Researchers find alternative pathways to HIV antibodies

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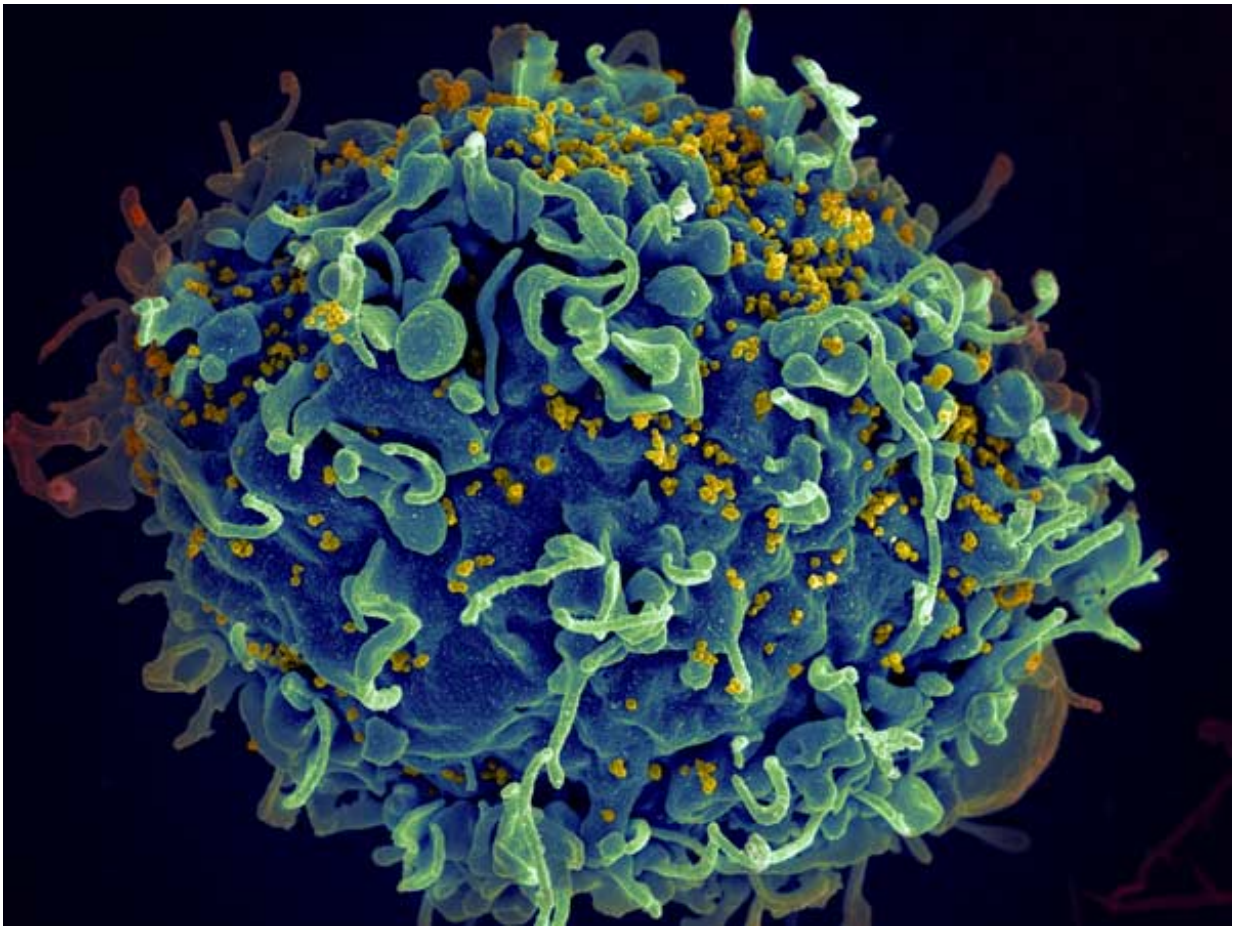

HIV (yellow) infecting a human immune cell. Credit: Seth Pincus, Elizabeth Fischer and Austin Athman, National Institute of Allergy and Infectious Diseases, National Institutes of Health

The immune system appears to hamper an investigational vaccine from inducing antibodies that protect against HIV infection, but there may be ways to overcome this impediment, according to research led by the Duke Human Vaccine Institute.

Using mouse and monkey models, the researchers showed they could could identify the roadblocks to inducing the broadly neutralizing antibodies that are considered imperative for successful protection against infection.

They then found alternative antibody pathways that approached the neutralizing capability of protective antibodies, setting the course for potential strategies to circumvent the immune system's response and enable the desired protection from a potential vaccine.

"This is the first demonstration of the extraordinary ability of the immune system to get around this process of thwarting the development of broadly neutralizing antibodies in mice and monkeys, and it is very helpful to us to begin to predict how the human immune system will respond," said Barton F. Haynes, M.D., director of the Duke Human Vaccine Institute. Haynes is senior author of a study published April 27, 2016, in the journal *Science Translational Medicine*.

Even in recombinant mice specially engineered to make broadly neutralizing antibodies when vaccinated with the experimental HIV vaccine, the immune system halts the process. Haynes said this reaction is a result of the virus's ability to mimic the host, causing the immune system to call off an attack rather than escalate it in a process known as immune tolerance.

When introducing the investigational vaccine in the mice, the antibody process was re-activated, but did not fully expand and develop.

In monkeys, the experimental vaccine induced a new type of antibodies, and demonstrated an alternative pathway to antibody neutralization.

"What we're hoping is that the investigational vaccine, which has been designed for human immune system, will do even better in humans than it has in monkeys," Haynes said. "We are working on ways to get around the final hurdle that's limiting the broadly neutralizing antibodies we want, but this is further than we have gotten before."

More information: R. Zhang et al. Initiation of immune tolerance-controlled HIV gp41 neutralizing B cell lineages, *Science Translational Medicine* (2016). DOI: 10.1126/scitranslmed.aaf0618

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