New technology opens gateway to studying HIV-specific neutralizing antibodies

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Many scientists believe a vaccine that prevents HIV infection will need to stimulate the body to make neutralizing antibodies, infection-fighting proteins that prevent HIV from entering immune cells. Previous research has shown that some individuals who control HIV infection without medication naturally produce antibodies able to neutralize diverse strains of HIV. Until now, however, scientists were hampered in studying the way effective HIV-neutralizing antibodies arise during natural HIV infection because scientists lacked the tools to obtain more than a few HIV-specific antibodies from any given individual.

A new research endeavor has assembled a group of state-of-the-art techniques for the first time to study the phenomenon of natural antibody-mediated HIV neutralization. The project demonstrates how this system can isolate dozens of HIV-specific antibodies from a single HIV-infected individual, something never accomplished before. Applied prospectively to a large group of HIV-infected individuals, the system will enable scientists to identify and define the diverse set of neutralizing antibodies that arise during natural HIV infection, information that may prove important in vaccine development.

John R. Mascola, M.D., Richard T. Wyatt, Ph.D., and Mark Connors, M.D., all of the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, participated in the research, which NIAID co-funded. Michel C. Nussenzweig, M.D., Ph.D., of The Rockefeller University led the team of 22 co-investigators in this collaboration.

The process begins with collecting memory B cells, which produce antibodies, from HIV-infected individuals previously screened for strong neutralizing antibody responses. These B cells are incubated with a specially flagged protein from the outer shell of an HIV virus particle. The HIV-specific memory B cells bind to the flagged protein, enabling researchers to identify these cells, isolate and store them. Then, for each of the HIV-specific memory B cells, a pioneering technique expresses the genes that code for HIV-specific antibodies. Finally, assays help scientists determine which of these antibodies can effectively neutralize HIV.

More information: JF Scheid et al. Broad diversity of neutralizing antibodies isolated from memory B cells in HIV-infected individuals. *Nature* DOI 10.1038/nature07930 (2009).

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