MedicalXpress

Mechanism found for development of protective HIV antibodies

July 24 2014

Scientists at Duke Medicine have found an immunologic mechanism that makes broadly neutralizing antibodies in people who are HIV-1 infected.

These findings, published online July 24, 2014, in the journal *Cell*, are a major development toward determining the key to induction of potent neutralizing antibodies by an HIV vaccine.

The research team found that two distinct B-cell lineage antibodies teamed up to stimulate the highly sought-after broadly neutralizing antibodies to HIV. The team was led by Barton Haynes, M.D., director of the Duke Center for HIV/AIDS Vaccine Immunology-Immunogen Discovery (CHAVI-ID) and the Duke Human Vaccine Institute, and John Mascola, M.D., director of the Vaccine Research Center of the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

The induction of these antibodies that can neutralize a variety of HIV strains is a key strategy for a global vaccine, Haynes said. High levels of such antibodies are made in approximately 20 percent of individuals with HIV infection.

Last year, this team published in the journal *Nature* the first mapping of co-evolution of broadly neutralizing antibodies (bnAbs) and the viruses that induced them in an infected individual. Now the same team reports the precise mechanism by which immune system B cells learn to neutralize many HIV strains.

In this new study, scientists were surprised to discover that a helper neutralizing set of antibodies cooperated with cross-reactive neutralizing antibodies to lead to a potent set of broadly neutralizing antibodies. The other helper lineage contained antibodies with neutralization for the virus that caused the infection.

This antibody targeted a virus outer coat (envelope) region to which the broad neutralizing antibodies also bound. In doing so, the helper lineage antibodies selected viruses with strong ability to stimulate the broadly neutralizing set of antibodies.

Thus, one set of antibodies selected a set of virus escape mutants that "taught" the broadly neutralizing lineage how to neutralize HIV variants. The scientists hypothesize that this process occurs iteratively throughout infection to lead to the ability to make antibodies that can neutralize a wide spectrum of HIV strains.

"The finding that the maturation of a bnAb lineage could be boosted by a helper lineage has significant implications for the development of AIDS vaccines," said one of the first authors, Feng Gao, M.D., of the Duke Human Vaccine Institute. "Repeated immunization of immunogens derived from the initial transmitted/founder virus and escape variants with higher binding ability to a bnAb lineage may be required to induce bnAbs."

"The next step is to perform similar studies in other individuals who make broadly neutralizing antibodies, and determine if this is a general mechanism for induction of other specificities of such antibodies," Haynes said. "Then the ultimate proof of utility of this discovery is to use it to design immunogens that can induce broadly neutralizing antibodies by vaccination."

Using the findings from this study, the team has designed vaccine

immunogens to selectively trigger the cooperating antibody-producing B cells to cooperate to make broadly neutralizing antibodies in a manner that mimics broadly neutralizing antibody development in natural HIV infection.

Provided by Duke University Medical Center