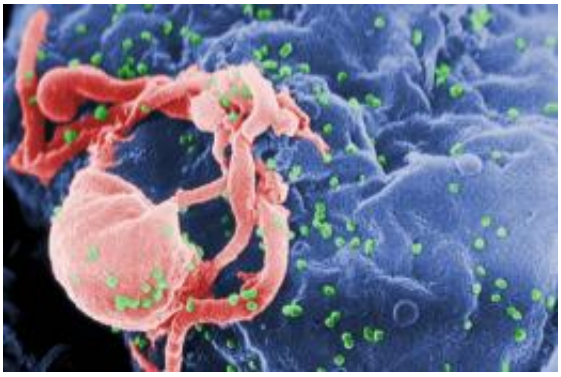
MedicalXpress

New research offers hope for HIV vaccine development

August 13 2014



Human immunodefieciency virus (HIV). Credit: C. Goldsmith/public domain

In a scientific discovery that has significant implications for HIV vaccine development, collaborators at the Boston University School of Medicine (BUSM) and Duke University School of Medicine have uncovered novel properties of special HIV antibodies. The paper, published in *Cell Host and Microbe*, describes how some HIV antibodies experience an unusual type of mutation, a phenomenon that allows them to neutralize many different strains of HIV. These antibodies are called "broadly neutralizing antibodies," or BNAbs.

Antibodies develop from immune cells known as B cells. When B cells are confronted with foreign elements (known as antigens), some of them experience a high rate of mutations resulting in the substitution of an amino acid within the antibody for another. B cells whose antibodies

carry variations that allow them to bind tightly with antigens proliferate, whereas those that do not die off. Thus, the immune system is able to adapt constantly by utilizing its own very fast version of evolution. More rarely, the antibodies will experience more dramatic changes than single amino acid substitutions. When whole strings of amino acids are inserted or deleted, this is known as an indel. Less than four percent of human antibodies contain indels; in BNAbs this figure is more than 50 percent. Only a small subset of HIV-infected individuals produce BNAbs.

Comparing the antibody genes of HIV infected and non-infected individuals, scientists discovered that HIV infected individuals had 27 percent more insertions and 23 percent more deletions than non-infected individuals. They also found this elevated rate of mutation persisted in all HIV-infected individuals, regardless of their ability to produce BNAbs. Most importantly, this high rate of indels was due to an overall increase in mutation frequency rather than something special associated with HIV itself, or unusual characteristics of the people who are able to make BNAbs. "This result suggests that a BNAb-eliciting vaccine is possible after all," explained lead and corresponding author Thomas B. Kepler, PhD, professor of microbiology at BUSM. "More than 80 percent of indels were found in genetic regions responsible for binding to the HIV virus," he added.

Since the BNAb indels don't result from special characteristics of the people who make them, the researchers suspected that the indels may be important for the antibody function. They studied one particular BNAb called CH31, which has a very large indel, to see what role these indels might have played in the acquisition of broad neutralizing activity. They found that the indel was the key event in the development of CH31. According to the researchers just putting the indel into antibodies that did not originally have it, increased its effectiveness eight-fold; taking it away from ones that did have it initially, made them much worse. "When tested on their ability to broadly neutralize HIV, only those CH31

antibodies with indels were able to accomplish the task," said Kepler.

Barton Haynes, MD, director of the Duke Human Vaccine Institute and senior author noted, The more we understand about the unusual pathway the BNAbs take to develop, the better chance we will have in inducing them. This news study unravels a particularly complex BNAb pathway." The great hope in the quest to prevent HIV-1 is the development of a single vaccine that can cover multiple forms of HIV-1. A vaccine that works by eliciting BNAbs is a major goal, and this new work suggest that strategies for such a vaccine should focus on speeding up the antibody evolution that occurs after every immunization. The study suggests that such a strategy could work in everyone, not just a lucky few.

Provided by Boston University Medical Center