Scientists find surprising trait in anti-HIV antibodies

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Authors of the new paper included (left to right) James Voss, Raiees Andrabi, Dennis Burton, Bryan Briney and Chi-Hui Liang. Credit: Cindy Brauer, The Scripps Research Institute

Scientists at The Scripps Research Institute (TSRI) have new weapons in the fight against HIV.

Their new study, published Nov. 17, 2015 as the cover article of the

journal *Immunity*, describes four prototype antibodies that target a specific weak spot on the virus. Guided by these antibodies, the researchers then mimicked the molecular structure of a protein on HIV when designing their own potential HIV vaccine candidate.

"This study is an example of how we can learn from natural infection and translate that information into vaccine development," said TSRI Research Associate Raiees Andrabi. "This is an important advance in the field of antibody-based HIV vaccine development."

Andrabi served as first author of the study, working in the lab of senior author TSRI Professor Dennis R. Burton, who is also scientific director of the International AIDS Vaccine Initiative (IAVI) Neutralizing Antibody Center and of the National Institutes of Health's Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery (CHAVI-ID) at TSRI.

Surprising New Antibodies

The findings build on the success of several recent TSRI studies showing that, with prompting, the immune system can develop antibodies to neutralize many strains of HIV.

In the new study, the researchers carried out a series of experiments involving virus modifications, protein and antibody engineering. They found that four antibodies targeted a single spot on HIV's surface called the V2 apex. This was significant because the V2 apex could be recognized by these antibodies on about 90 percent of known HIV strains—and even related strains that infect other species. A vaccine targeting this region could protect against many forms of the virus.

"This region helps stabilize the virus, so it's an important area to target if you want to neutralize HIV," said Andrabi.

Investigating further, the researchers noticed that two of the four antibodies had an unusual feature that could prove important in vaccine design.

The immune system usually begins its fight against infection by activating immune B cells that express 'germline' forms of antibodies, on their surface, to bind invading pathogens. Germline antibodies rarely bind viruses very effectively themselves; instead, they are precursors for more developed antibodies, which mutate and hone their response to the invader.

Yet in the new study, two of the antibodies did not need to mutate to bind with the V2 apex; instead, these antibodies used part of their basic germline structure, encoded by non-mutated genes. This means any patient with HIV should, in theory, have the ability to kick-start the right immune response.

Unfortunately, the immune system seems to naturally produce only a small number of these HIV-neutralizing germline antibodies. To generate an immune response that would favor these antibodies, it was critical for the scientists to find the right proteins in HIV that the antibodies could recognize and bind to.

In the new study, the researchers succeeded in mimicking a structure on HIV called the native HIV coat protein. This let them design proteins that do indeed bind well to the germline antibodies and hopefully start a useful immune response. The next step will be to test the vaccine candidates in animal models.

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