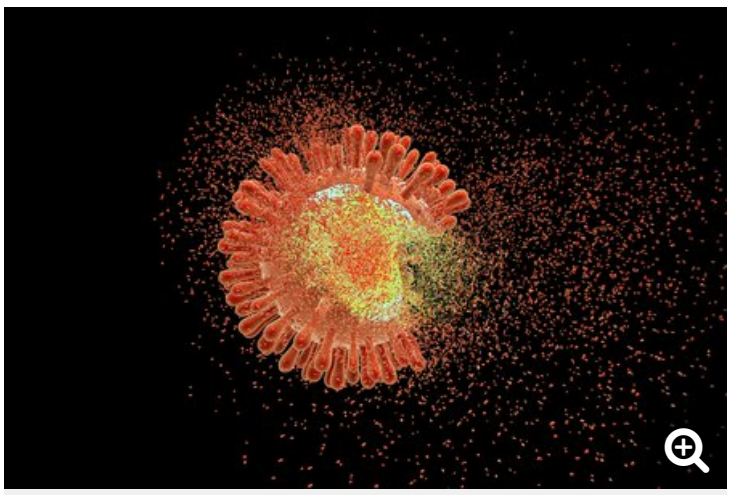
Progress Toward an HIV Vaccine

July 29, 2019

Two recent studies from Caltech characterize sites of vulnerability on the HIV virus and take a first step toward creating a vaccine. Ultimately, a vaccine for HIV would mean that the AIDS-causing virus could eventually be eradicated worldwide.



Credit: Shutterstock

The research is described in two recent papers from the laboratory of Pamela Björkman—the David Baltimore Professor of Biology and Bioengineering—and collaborators at The Rockefeller University.

How the Body Fights HIV

When exposed to an invading virus, the human immune system develops proteins called antibodies that become specialized to recognize and prevent infection by that particular virus. Generally, vaccines work by injecting a person with a piece of a virus—insufficient to cause illness but enough to induce the body to create antibodies to the virus. Should a person later be exposed to that particular virus, the antibodies would recognize and fight it.

HIV, though, is particularly difficult to combat. Thousands of HIV-1 variants have been characterized, and each can mutate rapidly to evade antibodies. Because HIV mutates throughout the course of an infection, the viruses inside an infected person make up a so-called viral swarm of different HIV strains, meaning that antibodies that can successfully combat one or even several strains are still unable to clear an infection. Though there are medications to manage the symptoms of HIV infection, an HIV vaccine would ensure that people would not get infected with HIV in the first place.

The ultimate goal of any HIV vaccine or treatment is to prevent new infections by blocking the entry of the virus into the target cells. To do this, our bodies make antibodies that target the HIV envelope protein, the sole viral protein on the surface of HIV. Different strains of HIV all have similar envelope structures, and human antibodies are specialized to attack specific regions of the envelope. For example, some antibodies target a site on the virus called the CD4 binding site (CD4bs), which is where HIV latches onto human cells to infect them. Because the CD4bs is so important for the virus's function, it is relatively similar—conserved—even across many HIV strains. If antibodies are to be broadly effective, it is ideal to target conserved regions like the CD4bs.

Discovering a New Gap in HIV's Defenses

Some individuals produce potent antibodies that are effective against many different strains of HIV. These are called broadly neutralizing antibodies, or bNAbs, for their ability to neutralize a broad spectrum of HIV viruses.

Working with collaborators at The Rockefeller University, Caltech researchers discovered a previously uncharacterized type of bNAb derived from an HIV-positive patient. The team found that this new antibody, named SF12, targets a region of the

Subscribe

Caltech Matters >

Share this

Tags

biological science & medicine

Related Links

> AN ANTIBODY THAT CAN ATTACK HIV IN NEW WAYS

> GENETICALLY ENGINEERED ANTIBODIES SHOW ENHANCED HIV-FIGHTING ABILITIES

> A DETAILED LOOK AT HIV IN ACTION

SEE ALL NEWS >

https://www.cce.caltech.edu/news-and-events/news/progress-toward-hiv-vaccine 1/3

HIV envelope called the silent face. This region of the envelope is called "silent" because it is usually not targeted by antibodies, or it is recognized only by antibodies that are not very potent and specific to certain strains. However, SF12 is effective in fighting at least 60 percent of all known HIV strains and neutralizes 100 percent of the HIV strains commonly found in Southeast Asia—strains that are poorly recognized by most other bNAbs.

The work suggests that the silent face is a promising target for designing vaccines and antibodies to fight HIV.

The First Step Toward a Vaccine

In another study also in collaboration with The Rockefeller University, Caltech scientists developed the first component of a possible HIV vaccine.

Because creating antibodies is a complex multistep process for the immune system, many vaccines must be given in several doses known as boosts. The first step in an HIV vaccine must induce the immune system to create bNAb precursors, crucial younger versions of antibodies that will eventually mature into powerful bNAbs. An imprecise precursor will lead to an ineffective antibody.

The researchers aimed to develop an initial vaccine that would induce mice and nonhuman primates to produce bNAb precursors that would specifically target a certain region on the HIV envelope called V3. Certain features of V3 are found among a wide variety of HIV viruses, and thus it is a good target for robust bNAbs.

The team first engineered a piece of the HIV envelope to remove some sugars, called glycans, that HIV uses to shield vulnerable regions like V3 from antibodies. After exposing V3, the researchers *added* glycans to other regions that are more variable between strains, covering them up in order to ensure that the test animals would produce antibodies specific to the V3 region. Then, the team placed about 70 of these identical engineered envelopes (containing no viral genetic material) on a carrier particle and injected this into the animal models.

Indeed, this engineered complex caused the animals to create the correct bNAb precursors specific to the V3 region on HIV. Adding the engineered envelope to the carrier particle ensured a large response from the animals' immune systems. When exposed to a real HIV virus, the precursor bNAbs developed by this initial inoculation were able to see past the virus's shielding glycans to target its vulnerable regions.

The team is now working on developing the next doses of the vaccine that would enable precursors to mature into bNAbs.

Study Details

The first paper appeared online on May 21 in the journal *Immunity* and is titled "Broad and Potent Neutralizing Antibodies Recognize the Silent Face of the HIV Envelope." Caltech postdoctoral scholar Christopher Barnes is a co-first author along with Till Schoofs of The Rockefeller University. In addition to Barnes and Björkman, other Caltech co-authors are Nina Suh-Toma, a former high school student volunteer in the Björkman laboratory; senior research specialist Anthony P. West, Jr. (PhD '98); and associate research technician Yu Erica Lee. Additional co-authors are Jovana Golijanin, Lilian Nogueira, and Michel C. Nussenzweig of The Rockefeller University; Philipp Schommers, Henning Gruell, and Florian Klein of the University of Cologne and the German Center for Infection Research; Franziska Bach of the University of Cologne; Ivelin S. Georgiev of Vanderbilt University; Robert T. Bailer, John R. Mascola, and Nicole A. Doria-Rose of the National Institutes of Health; Julie Czartoski and M. Juliana McElrath of the Fred Hutchinson Cancer Research Center; and Michael S. Seaman of Harvard Medical School. Funding was provided by the National Institute of Allergy and Infectious Diseases (NIAID), the National Institutes of Health (NIH), the Bill and Melinda Gates Foundation Collaboration for AIDS Vaccine Discovery, the NIH Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery, the European

Research Council, the German Center for Infection Research, the Vaccine Research Center of the NIAID/NIH, the Ernst Jung Career Advancement Award for Medical Research, the National Center for Advancing Translational Science Award program, the DZIF, the Hanna Gray Fellowship Program from the Howard Hughes Medical Institute, and the Burroughs Wellcome Fund.

The second paper appeared online on May 29 in the journal *Nature* and is titled "Immunization expands B cells specific to HIV-1 V3 glycan in mice and macaques." Caltech research scientist Harry Gristick (PhD '15) is a co-first author along with Amelia Escolano of The Rockefeller University. In addition to Gristick and Björkman, other Caltech co-authors are graduate student Morgan E. Abernathy; Anthony P. West, Jr.; Christopher Barnes; graduate student Alexander A. Cohen; former graduate student Haoqing Wang (PhD '19), now of Stanford University; research scientist Jennifer R. Keeffe (PhD '09); research technician Han Gao; and research technician Alisa V. Voll. Co-authors from The Rockefeller University are Julia Merkenschlager, Thiago Y. Oliveira, Joy Pai, Jovana Golijanin, Daniel Yost, Zijun Wang, Kai-Hui Yao, Jens Bauer, Lilian Nogueira, Anna Gazumyan, and Michel Nussenzweig. Additional co-authors are Rajeev Gautam and Malcolm A. Martin of the National Institutes of Health; Peng Zhao and Lance Wells of the University of Georgia; David C. Montefiori of Duke University; Michael Seaman, Murillo Silva, and Darrell J. Irvine of MIT; and Andrew T. McGuire and Leonidas Stamatatos of the Fred Hutchinson Cancer Research Center and the University of Washington. Funding was provided by the NIAID, the NIH, the National Center for Biomedical Glycomics, the Bill and Melinda Gates Foundation Collaboration for AIDS Vaccine Discovery, the Robertson Fund of the Rockefeller University, the National Science Foundation, EMBO, the HHMI Hanna Gray Fellowship, and the Burroughs Wellcome Fund.

WRITTEN BY
Lori Dajose

CONTACT
Lori Dajose
(626) 395-1217
ldajose@caltech.edu