



# New HIV Vaccine Shows Unprecedented Success in Preclinical Study

Vaccine approach yields high numbers of HIV-neutralizing antibodies in monkeys.

July 8, 2026 By Madeline McCurry-Schmidt and La Jolla Institute for Immunology

---

## Highlights:

- Scientists at La Jolla Institute for Immunology and Scripps Research have developed an HIV vaccine that trains immune cells to see past HIV's defenses.
- This HIV vaccine works by prompting the body's immune system to make substantial numbers of rarely seen broadly neutralizing antibodies.
- In this new study, this vaccine resulted in the best HIV-fighting antibody response ever seen in primates. Human trials have now started.

La Jolla, CA — A new HIV vaccine developed by La Jolla Institute for Immunology (LJI), Scripps Research scientists, and IAVI has the potential to protect humans from developing HIV infection and AIDS. This HIV vaccine is the first to generate a high number of “broadly neutralizing,” virus-fighting antibodies in primates.

“This feels like a huge success,” says LJI Professor and Chief Scientific Officer [Shane Crotty, PhD](#), who co-led the research with Scripps Research Professor [William Schief, PhD](#). “We constructed a successful vaccine from the ground up, which required a deep understanding of the immune system.”

This groundbreaking research, published in [Nature](#), is the result of 14 years of collaboration between La Jolla Institute for Immunology and Scripps Research, as part of the Scripps Consortium for HIV/AIDS Vaccine Development (CHAVD). “This has been one of those Apollo moon mission-type projects, where there is an exceptional goal and the team has to accomplish a myriad of discoveries and inventions along the way,” says Crotty.

## Outsmarting HIV

The new vaccine works by intervening in a process called B cell maturation. B cells make antibodies. Like many immune cells, B cells have an early “naive” stage before they are ready to make antibodies. B cells start to mature once they get the signal that a pathogen, such as a virus, is trying to attack. B cells see pieces of that pathogen’s molecular structure and start producing antibodies that can bind to that structure and halt infection.

It can take a little while for B cells to find the right “bullseye” on a pathogen. But B cells keep trying. As they mature, B cells tweak their antibody production, refining antibody structures to bind to a pathogen in just the right, vulnerable spots.

Scientists describe B cell development as a training process or bootcamp. In most cases, the body is left with a well-honed B cell army.

HIV is hard to beat because it doesn’t give B cells a chance to develop effective antibodies. The first problem is that HIV disguises itself from the immune system. The virus is wrapped in an ever-shifting cloak of sugar molecules, called glycans. This lets HIV sneak undetected past human cells, which are also covered in glycans.

The second big problem is that HIV mutates very quickly. “The worldwide diversity of HIV mutations is extraordinary. Even the diversity within one individual person living with HIV is dramatic,” says LJL Instructor Patrick Madden, PhD, who served as study co-first author with Jon Steichen, PhD, an institute investigator at Scripps Research.

The third problem is that HIV changes its shape when it infects human cells. Even if B cells get a glimpse of its viral structure—snap!—the structure changes.

Taken together, these problems rarely give B cells a chance to hone their antibody responses against HIV. Even if a B cell manages to make neutralizing antibodies, the virus can mutate or change its shape, rendering those antibodies useless.

The LJL and Scripps Research teams spent years hunting for “broadly neutralizing” antibodies that can actually bind to HIV and recognize key viral structures, even if the rest of the virus mutates. These antibodies are very, very rare, but they can be found in blood samples from a small number of people living with HIV.

An effective HIV vaccine would need to prompt the immune system to make these same broadly neutralizing antibodies. “How could we flip the whole immune response on its head so the rare responses become the common responses? That was a critical challenge we faced,” says Crotty.

## Testing the New Vaccine

It was time to go back to B cell bootcamp. The scientists studied what made the HIV-fighting B

cells special. Then they reversed the process to see exactly how those B cells matured. By looking back at the maturation process, the researchers could track how the B cells changed when they saw specific pieces of the HIV structure.

The team discovered that B cells matured to make broadly neutralizing antibodies after they got an early look at parts of HIV's outer "envelope" protein. Because these viral sites sparked an immune response, scientists would call them "antigens."

An effective HIV vaccine would likely need to include models of these antigens. The antigens would work like mugshots of America's most wanted. If B cells saw those antigens early and often, they would get really good at recognizing and even neutralizing HIV. "We were trying to mimic the progression of those neutralizing antibodies," says Madden.

In a feat of molecular engineering, the Schief Lab developed vaccine molecules that resembled the real HIV antigens. The scientists then worked with Emory National Primate Research Center, to test this potential HIV vaccine in a non-human primate species called rhesus macaques.

The researchers first administered a "priming" vaccine meant to activate each animal's naive B cells. The animals then received a series of "shepherding" booster shots to help their B cells develop along the right path.

"This series of vaccinations will guide, or 'walk', a B cell from its naive state to its broadly neutralizing state," says Madden.

This new type of vaccine approach is called "germline targeting" because it targets naive B cells in their "germline" or naive form, before they begin their training process.

The scientists found that around 44% of the animals went on to produce broadly neutralizing antibodies against HIV in their blood. These antibodies were impressively abundant.

"We succeeded in taking ultra-rare antibody responses and turning them into common responses by the end of the vaccination process," adds Crotty. In other research recently published, they reported a new strategy to accelerate related vaccine antibody responses [[See Nature Immunology paper](#)].

The team didn't test whether these antibodies could prevent infection, but it's significant that these antibodies could be found in the blood, where they could encounter and potentially block HIV.

### Bringing the HIV Vaccine to Humans

The Crotty Lab plans to investigate how they might change the booster shot regimen to make the HIV vaccine even more effective. "It was incredible to get those results, but of course we'd like to see a response in 100% of the animals," says Madden.

Importantly, the antibodies found in the animal subjects resembled the exact kinds of broadly neutralizing antibodies seen in those rare humans who made their own neutralizing antibodies. It's clear that our immune systems can make these powerful antibodies, given the right training.

"We believe this vaccine approach is even more likely to succeed in humans, because of the immunogenetics," Crotty says.

The priming immunogen used in this study was evaluated in humans in the HVTN 144 trial and is currently being tested in the [Phase I trial IAVI G004](#). IAVI, Scripps Research, the [HIV Vaccine Trials Network](#), and partners are now advancing plans to further evaluate the full immunization regimen in a future human clinical study.

Additional authors of the study, "[Vaccination elicits HIV broadly neutralizing antibodies in primates](#)," include Claudia T. Flynn, Swastik Phulera, Monolina Shil, Oleksandr Kalyuzhniy, Alessia Liguori, Carolyn Kifude, Leigh M. Sewall, Christopher A. Cottrell, Krystal M. Ma, Sabyasachi Baboo, Jolene K. Diedrich, Katherine McKenney, Allan C. deCamp, Diane G. Carnathan, Ivy Phung, Parham Ramezani-Rad, Ester Marina-Zárate, Brian Freeman, Zhenfei Xie, Jeong Hyun Lee, Troy Sincomb, Nicole Phelps, Danny Lu, Diana Goodwin, Ryan Tingle, Yumiko Adachi, Nushin Alavi, Jenny Tran, Andy S. Tran, Alyne Nascimento, Catherine Sovie, Daniel L. V. Bader, Hannah Voic, Xiaoya Zhou, Grace Pixton, Agnes Walsh, Mariane B. Melo, Torben Schiffner, Facundo D. Batista, Dennis R. Burton, Darrell J. Irvine, James C. Paulson, John R. Yates III, Gabriel Ozorowski, Andrew B. Ward, Guido Silvestri.

This work was supported by National Institute of Allergy and Infectious Diseases (NIAID), of the National Institutes of Health, through grant UM1 AI100663 to the Scripps Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery (CHAVI-ID), grant UM1 AI144462 to the Scripps Consortium for HIV/AIDS Vaccine Development (CHAVD), P51 OD011132 to Emory National Primate Research Center, and R01 AI113867; by the Gates Foundation under the Collaboration for AIDS Vaccine Discovery (NAC INV-007522, INV-008813, INV-034657, and INV-064772), via the IAVI Neutralizing Antibody Center (NAC); and by the National Institute of Health grant S10OD025052.

This [news release](#) was published by the La Jolla Institute for Immunology on July 6, 2026.