The Rare Super-Antibodies That Destroy HIV

A recent study sheds new light on a rare immune response to the virus—and could bring researchers a step closer to developing a vaccine.

When a person becomes infected with HIV, the immune system kicks into gear: Immune cells called B cells build antibodies, tiny protein warheads that seek out and destroy viruses. But because HIV mutates so rapidly, these antibodies are generally ineffective—by the time B cells learn to build antibodies against one version of HIV, a new viral mutant has already taken
In some patients, the immune system manages to make antibodies that actually work against a broad spectrum of HIV mutants, but those antibodies typically emerge only five or six years into the infection. And by that point, their efforts may be too little, too late. “Once you already have an established infection with millions or billions of viral particles in an infected individual, even with a potent antibody response, it’s too late to shut everything down,” explains Satish Pillai, a researcher at the Blood Systems Institute of San Francisco.

These more effective antibodies can’t reverse the damage done to other immune cells over the preceding several years, but they can reduce the virus’s numbers and slow down the progression of the infection. Researchers have long speculated that if they kicked in early, they may be able to prevent HIV from gaining a toehold in newly infected individuals. But without knowing where these elite antibodies come from, it’s hard to pursue the idea much further.

A recent breakthrough may help to change that. In a study recently published in the journal *Cell*, a team led by Barton Haynes, an HIV researcher at Duke University, was able to track the evolution of HIV antibodies in individual who had been infected several years earlier. The team collected samples of the patient’s blood at 17 different points over the years to see how the B cells had mutated in response to the changing virus.

With each sample, the researchers ran the patient’s antibodies through an extensive battery of tests to assess their HIV-killing talent. One particular group of antibodies, called the CH235 lineage, stood out: The CH235s already exhibited a knack for finding and binding to a wide range of HIV mutants early in the infection; however, they didn’t master the “destroy” part of their “search-and-destroy” mission until after about five years after
infection. By then, the CH235 lineage could kill about 90 percent of the different types of HIV it encountered.

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“Anytime an antibody can kill 90 percent of HIV, I think that’s extraordinary,” says Peter Kwong, a researcher at the National Institutes of Health and one of the study’s co-authors. Kwong’s lab used a technique called x-ray crystallography to capture high-resolution portraits of each stage of CH235’s evolution. Kwong calls the paper a “creation story,” the first time they’ve been able to track an anti-HIV antibody from its “birth.” With every atom in CH235 accounted for, the researchers may be able to “train” uninfected people’s immune systems to produce the most potent version of CH235 through a series of vaccines.

Since 1987, more than 30 potential HIV vaccines have entered clinical trials, according to the World Health Organization, but many attempts have backfired often because of HIV’s enormous variability. A vaccine that boosts the body’s ability to make generalist antibodies like CH235s could be a more effective approach. “If you have a potent, broad antibody response, it should be able to snuff out that little bit of virus as it comes in the door,” says Pillai, who was not involved in the study. “One of the challenges in the field is figuring out how to induce these special antibodies.”

Moving forward, Kwong and Haynes say they plan to use these findings to develop a preventative HIV vaccine, or more likely, a series of vaccines that will start during childhood. “Until you have that very detailed structural and genetic record” of the antibodies that successfully attack the virus, Kwong says, “a lot of what we’re doing [in HIV vaccine development] is guessing.”
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