

Scientist identifies helper cells that trigger potent responses to HIV

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A major new finding that will significantly advance efforts to create the world's first antibody-based AIDS vaccine was published today by researchers from the La Jolla Institute for Allergy and Immunology.

La Jolla Institute scientist Shane Crotty, Ph.D., a respected vaccine [researcher](#) and member of one of the nation's top AIDS vaccine consortiums, showed that certain helper T cells are important for triggering a strong antibody response against HIV, the virus that causes AIDS. Helper T cells are disease-fighting [immune cells](#) key in shaping the body's response to [viruses](#) or other pathogens. The cells are multi-faceted, come in various types, and have numerous functions, including assisting with [antibody production](#).

"We've shown that a specific type of these cells, known as follicular helper T (Tfh) cells are not only necessary, but are a limiting factor that differentiates between an average and a potent antibody response to HIV," says Crotty, a scientific [collaborator](#) with the Center for HIV/AIDS Vaccine Immunology & Immunogen Discovery (CHAVI-ID), a major research consortium led by The Scripps Research Institute.

Notably, Crotty showed that the frequency of the Tfh cells correlated with development of broadly neutralizing antibodies against HIV in a large group of HIV-infected individuals. The International AIDS Vaccine Initiative put together the group of study participants, and collaborated on the analysis.

Dennis Burton, Ph.D., a prominent HIV expert who heads the CHAVI-ID consortium at Scripps, calls the finding "the kind of fundamental basic research that will eventually allow us to defeat HIV."

"Shane Crotty and his collaborators have made an important step in understanding how potent antibodies to HIV can be made, a step which is vital to the effort to develop an AIDS vaccine given that antibodies are critical to most successful vaccines," says Burton. "Crotty is a world expert on the cells that control antibody production and, by teaming up with AIDS researchers, he and his group have shown how these cells can be tracked in blood and provided evidence of their importance in generating the right types of antibody to HIV."

The findings were published online today in the journal *Immunity* in a paper entitled, "Human circulating PD-1+CXCR3-CXCR5+ memory Tfh cells are highly functional and correlate with broadly neutralizing HIV [antibody responses](#)."

Antibodies may be thought of as the body's smart bombs, which seek out infectious agents and tag them for destruction. Twenty-six human vaccines currently exist worldwide, 24 of which work by triggering the production of antibodies. Tfh cells are a type of CD4+ T helper cells specialized in providing help to B cells, which are the cells that make antibodies. "Essentially it's the Tfh cells that tell the B cells to produce antibodies," explains Crotty.

No vaccine currently exists for HIV (human immunodeficiency virus) and there is no cure for AIDS (acquired immune deficiency syndrome), which currently infects 34 million around the globe. While AIDS drugs have extended the lives of many sufferers, AIDS remains a major killer, particularly in developing countries, making the search for an effective HIV vaccine a public health priority.

In his study, Crotty used blood samples from HIV-infected patients and a control group of people without the disease. As part of his findings, Crotty also developed a robust test for identifying phenotypic markers for Tfh cells in the blood, a major new tool for AIDS researchers. "We found that rare HIV-infected individuals that made outstanding antibodies against HIV had higher levels of a particular kind of Tfh cells circulating in their blood than most people," he says. Further, the study showed a direct correlation between levels of Tfh cells and antibody response. "The higher the levels of Tfh cells, the more significant the antibody response," says Crotty.

Crotty says the ability to measure Tfh cells in the blood will assist AIDS vaccine researchers by serving as an indicator of antibody response. "The question has been, 'how do we make a vaccine that will stimulate those broadly neutralizing antibodies?' The need to elicit Tfh cells is one key piece of that puzzle."

The discovery is Crotty's latest major finding regarding the Tfh cells. In 2009, he drew national attention with his discovery, published in *Science*, illuminating a pivotal piece of the body's mechanism for switching on the production of antibodies. He proved that the BCL6 gene was like an on and off switch, or master regulator, that triggered the production of Tfh cells, which in turn told the B cells to make more antibodies. This seminal finding led to his recognition as an important scientist in vaccine design, and to his inclusion as a T cell expert in the CHAVI-ID vaccine consortium.

The consortium was one of two nationwide funded by the National Institutes of Health in 2012 in the face of new evidence from The Scripps Research Institute and others that an antibody-based HIV vaccine could be successful.

"For a long time, it wasn't thought possible," explains Crotty. "This was

due to a belief that humans just don't make good antibodies against HIV and also because the [virus](#) is extremely changeable." But over the years rare individuals began to turn up who appeared capable of making strong antibody responses against HIV. Researchers at Scripps and other institutions began testing blood samples from these individuals in animals and found that they were producing broadly neutralizing antibodies capable of eliminating most of the HIV varieties, says Crotty. Current estimates are that only about five percent of AIDS patients can produce these potent antibodies to HIV, and only multiple years after infection.

In the CHAVI-ID consortium at Scripps, vaccine experts from across the country are collaborating to create an HIV vaccine that will trigger these strong, protective antibodies before infection. The consortium is using an integrated two-pronged approach, with one research group focusing on antibodies and B cells, and the other group exploring the role of T cells in helping B [cells](#) produce [antibodies](#), which is Crotty's area of focus.

Provided by La Jolla Institute for Allergy and Immunology

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