

New HIV vaccine trial first to target dendritic cells

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When HIV was first discovered to cause AIDS in 1981, prominent scientists expected to have an effective vaccine within a couple of years. Three decades later, the disease has killed more than 25 million people and defied every effort so far to inoculate against it. But researchers at Rockefeller University are launching a new clinical trial that they hope will mark a turning point in the struggle to develop an effective vaccine against the deadly disease. Building on more than 15 years of research, they are testing a first of its kind vaccine that directly taps the power of the cells that orchestrate the body's immune response, called dendritic cells.

"We have good reason to believe that this novel effort targeting dendritic cells could significantly improve the quality of the [immune response to HIV](#)," says Sarah Schlesinger, associate professor of clinical investigation, who is leading the study.

Dendritic cells were originally discovered in 1973 at Rockefeller by Zanvil A. Cohn and Ralph M. Steinman, now head of the Laboratory of Cellular Physiology and Immunology. Over the years, these cells have been shown to coordinate the immune response, processing foreign substances like viruses or other infections and training the immune system's [T cells](#) to kill them. "We know that every vaccine works through dendritic cells in some way, we just haven't fully understood how," Schlesinger says. "Now we're going straight to the source."

The researchers are able to target dendritic cells because of a distinctive

marker on the [cell surface](#), a receptor called DEC 205, which was discovered about 12 years ago by Schlesinger's colleague and Steinman's former student Michel C. Nussenzweig, head of the Laboratory of Molecular Immunology. The team has engineered a powerful antibody, called a monoclonal antibody, to seek out DEC 205 and deliver a synthesized piece of an HIV protein. They have also incorporated a special molecule, called an adjuvant, that will spur dendritic cells to grow into their fully matured, disease-fighting state. In theory, these [dendritic cells](#) then will tell the immune system to seek and destroy anything containing that synthesized HIV [protein](#) - in other words, HIV, wherever it is found in the body. "This trial is the culmination of at least 15 years of laboratory research," Schlesinger says. "We're very excited to try it out."

Vaccines must go through three stages of clinical trials before they can be licensed for use by the U.S. Food and Drug Administration. The first, following extensive testing in laboratory and animal studies, tests for safety and tolerability in humans; the second gauges whether the vaccine is creating the immune response that is desired; only the third phase, which involves thousands of patients, costs tens of millions of dollars and can take a decade or longer, establishes whether the candidate is truly effective.

The trial at Rockefeller is in the first 'safety' stage, but researchers intend to probe many questions about whether or not it is effective as well. "We wouldn't want to put this into people without learning as much as we can about what kind of immune response it is generating," Schlesinger says.

To date, only three vaccine candidates have made it to the third stage of testing. The first two failed, making some scientists pessimistic about whether a vaccine could be developed at all. But results from the third trial, conducted in Thailand, gave new cause for hope when they were

released last fall. Even though a relatively small percentage of people were protected, it was at least proof for the potential of an effective vaccine. "It really gave the field a boost of momentum," Schlesinger says.

Researchers at Rockefeller are now recruiting 45 volunteers, ages 18 to 60, who are in good health and at low risk for acquiring HIV. Volunteers will visit Rockefeller 17 times over approximately 16 months, receiving the vaccine on three visits and giving a small blood sample each time. To help offset the costs of time and transportation, volunteers will receive \$100 per visit.

"What we can learn from the people who participate in this trial is absolutely invaluable to the vaccine development process," Schlesinger says. "Our hope is that it will teach us how we can change and improve on this candidate in order to develop a vaccine that we can move on through stage two and three trials and eventually help end this epidemic."

More information: To find out if you are eligible to participate in this study, contact Sarah Pollak, RN, at 212-327-7394.

Provided by Rockefeller University

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