HIV vaccine trial set for next year

Work led by San Diego researchers primes immune system for response

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A trial of a new HIV vaccine is expected to begin late next year (http://www.eurekalert.org/emb_releases/2016-03/sri-fih032316.php), based in part on a study led by scientists from The Scripps Research Institute and the La Jolla Institute for Allergy & Immunology.

The preliminary trial aims to start preparing the immune system to produce antibodies that neutralize a broad range of HIV, a virus that comes in incalculable variations that to date have defeated any vaccine thrown at it.

The study was published Thursday in the journal Science, available online at j.mp/hivtrial (http://j.mp/hivtrial). It found that 96 percent of humans have immune cells that respond to a potential vaccine component, a protein called eOD-GT8 60mer. The component prepares certain antibody-making cells called B cells to produce these powerful broadly neutralizing antibodies.

This early-stage vaccine isn't expected to be sufficient in itself to defeat HIV. But it will lay the foundation to further prepare the immune system to make these antibodies quickly, said Carl Dieffenbach, director of the National Institute for Allergy and Infectious Diseases, part of the National Institutes of Health.

Broadly neutralizing antibodies are found in about 20 percent of those infected with HIV, Dieffenbach said. But it can take years for the immune system to learn how to make them. By that time, the virus is too firmly established to eradicate.

The ultimate goal is a vaccine that allows those immunized to make these antibodies fast enough to stop the virus in its tracks.

Vaccine developers say a series of immunizations may be needed, each taking the immune system one step further down the road to a complete defense.

The eOD-GT8 60mer protein represents the first HIV antigen that prepares the "naive" B cells to prep for making broadly neutralizing antibodies, said Shane Crotty, a La Jolla Institute researcher. Crotty and TSRI's William Schief are senior authors on the study. The first co-authors are TSRI's Joseph Jardine, Daniel Kulp, Colin Havenar-Daughton, Anita Sarkar, Bryan Briney and Devin Sok.

Scientists have tried to develop an effective HIV vaccine for decades, with no success to date. That's because HIV mutates extremely rapidly, and the parts that mutate on the surface are the ones that draw the immune system's attention, Dieffenbach said.

The virus does have vulnerable "conserved" regions necessary for infection, but these are well hidden. That's why it can take years for the immune system to identify them, and in people called "elite controllers," keep the virus in check. These elite controllers may show no obvious symptoms of HIV, even without therapy.

However, the immune system has never naturally eradicated HIV from the body once it's established, Dieffenbach said. That's because HIV is a retrovirus, capable of copying its genome into the genome of the immune cells it parasitizes. Once incorporated into the host genome, HIV can lie low and evade immune system attacks.

The discovery of broadly neutralizing antibodies, pioneered by TSRI's Dennis Burton, provided a new insight into how to thwart HIV, Crotty said. Since 2009, Burton, a study co-author has been collecting these antibodies from those infected. Studying them has revealed unexpected vulnerabilities in HIV that Burton and colleagues have used to reverse-engineer how the immune system makes these antibodies.

Antibody-making cells begin with approximations of a response, and through trial and error, "learn" how to make ones progressively better at attacking infectious agents such as HIV. So scientists at TSRI, La Jolla Institute and other centers across the country have collaborated on studying the details of how these broadly neutralizing antibodies are made.

Working backwards, the scientists characterized these broadly neutralizing antibodies, which are the final products of the immune response, the properties of the cells that make them, and the predecessors of these cells.

Finally, in the new paper in Science, researchers have identified certain B cells that make one class of these broadly neutralizing antibodies. These cells are extremely rare, about 1 in 2.4 million B cells, Crotty said. Moreover, the scientists also designed an antigen that efficiently turns these rare B cells into those that make predecessors for one class of these broadly neutralizing antibodies.