Study finds unique HIV vaccine formula elicits strong immune responses

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Today, Advanced BioScience Laboratories, Inc. and the University of Massachusetts Medical School report that their unique HIV vaccine formulation was effective in eliciting strong and balanced immune responses in healthy human volunteers.

The findings are published in the journal *Vaccine* ("Cross-subtype antibody and cellular immune responses induced by a polyvalent DNA prime–protein boost HIV-1 vaccine in healthy human volunteers," *Vaccine* online, May 22, 2008) In light of these initial findings, additional assays on volunteers' samples were done by researchers at the University of Alabama at Birmingham, independently confirming the presence of long lasting and high quality T cell responses against HIV antigens. Results from this confirmatory study are currently available online in the *Journal of Virology* (April 30, 2008).

In this phase I clinical trial, sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), volunteers first received three injections of a DNA vaccine which expresses protective antigens from the HIV virus, followed by two injections of a protein vaccine whose components matched those included in the DNA vaccine. The report in *Vaccine* is the first scientific article in which a "DNA prime-protein boost" combination vaccination method is tested in humans for HIV vaccine development. Scientists at ABL and UMMS and their collaborators discovered that this combination approach is highly effective in inducing strong antibody and cell-mediated immune responses in human volunteers.

“Given the challenges of developing a vaccine against HIV, scientists have long believed that a final, effective HIV vaccine will require the induction of balanced responses from both arms of human immune system. Our results demonstrate that it is feasible to use this combination approach to achieve this objective,” said Phillip Markham, PhD, of ABL, the Principal Investigator (PI) on this vaccine development effort, performed under contract to the NIAID.

One unique design underlying this combination HIV vaccine formulation is the use of a “cocktail” of five different envelope (Env) proteins collected from HIV viruses circulating in different parts of the world. Env is a key protective antigen and the goal was to elicit broad antibody responses against a wide range of HIV viruses in order to counter the issue of frequent HIV mutations. Indeed, the high titer antibodies found in volunteers’ sera were able to recognize each of a very diverse group of Env antigens that were included in this study. More significantly, the majority of volunteers developed positive neutralizing antibodies against a good portion of the five HIV subtypes included in the assay.

Shan Lu, MD, PhD, professor of medicine and biochemistry & molecular pharmacology at the University of Massachusetts Medical School and the co- Principal Investigator (co-PI) of the vaccine development program, describes the finding of neutralizing antibodies in this study as “a major step forward.”

“Previously, we didn’t know where to start. The neutralizing antibody titers in our study are still relatively low, but, these results are promising and open the door for future efforts to optimize HIV vaccine formulations in order to achieve a protective HIV vaccine,” said Dr. Lu.

The dominant approaches in the current HIV vaccine field rely on viral vector-based delivery systems, an approach that produced disappointing results in a recent efficacy trial. Drs. Markham and Lu believe their HIV

vaccine strategy will offer an alternative approach to focus on the induction of protective antibodies for HIV vaccine development, while maintaining strong cell-mediated immune responses. In addition to NIH, the International AIDS Vaccine Initiative (IAVI) also provided funding support to part of the study. Researchers from Duke University Medical School also participated, as did Dr. Paul Goepfert at the University of Alabama-Birmingham.

Source: University of Massachusetts