Ho: Enhancing Innate Immune Activation

OVERVIEW

The Ho-led research consortium is exploring ways to enhance immune activation upon vaccine administration. Dendritic cells (DCs) are a type of immune system cell involved in the body's innate response to pathogenic invaders. These cells ingest viral particles and display bits of them on their surfaces so that other immune cells, such as T-cells, can mount immune responses to the viruses. The Ho-led team is studying various approaches to harness the power of these dendritic cells to improve vaccine immunogenicity both in pre-clinical and clinical research efforts.

RESEARCH OBJECTIVES

The Ho-led research team is pursuing several distinct vaccine approaches to direct HIV-1 antigens to dendritic cells or induce type I interferon that can recruit and mature DCs. Each of these vaccine approaches has a modality to mature DCs, either co-administered exogenously or built-in.

The team is also developing both a novel vaccine adjuvant and a novel vaccine delivery platform. The adjuvant is a glycolipid compound that stimulates natural killer T cells, leading to DC maturation and improved immune responses to vaccines. In a parallel effort, the TriGridTM *in vivo* electroporation device improves the immunogenicity of DNA-based vaccines by increasing the amount of vaccine delivered to cells.

These product development activities entail studies ranging from *in vitro* construction and characterization to animal experimentation, and to pilot human trials for select efforts.

PROGRESS

Researchers at the Aaron Diamond AIDS Research Center (ADARC) have successfully completed the first Phase 1 clinical trial of ADVAX, a DNA-based HIV vaccine candidate delivered with the TriGridTM *in vivo* electroporation system, manufactured by Ichor Medical Systems, in healthy volunteers. Strong positive results indicate that in vivo electroporation is safe, tolerable, enhances the cellular immunogenicity of ADVAX, and is dose-sparing. Ancillary immunogenicity studies indicate that ADVAX delivered by electroporation not only enhances the magnitude of cellular immune responses to this DNA vaccine candidate, but also its breadth.

Researchers have also identified a promising new glycolipid-based vaccine adjuvant, 7DW8-5, which significantly enhances the immunogenicity of DNA and adenovirus-based vaccines in a mouse model. In partnership with the U.S. Naval Medical Research Center (NMRC) and the Tulane National Primate Research Center (TNPRC), we demonstrated that this glycolipid-based adjuvant can significantly boost the immunogenicity of an Ad5-based vaccine candidate in monkeys without causing evident systemic reactogenicity. We are currently engaging in GMP-manufacture and release testing of the 7DW8-5 drug product in anticipation of a Pre-IND meeting with the US FDA in the next quarter and a Phase 1 clinical trial that will begin enrollment at the end of next year.

Grant at a Glance

Principal Investigator

David Ho, MD

Grantee Institution

Aaron Diamond AIDS Research Center, New York, USA

Project Title

Harnessing Dendritic Cells & Innate Immune Activation Signals to Guide HIV-1 Vaccine Development

Grant Award

$24.7 million over 6 years, awarded July 2006

Collaborating Institutions

- Mount Sinai School of Medicine, USA
- The Rockefeller University, USA

External Scientific Advisory Board

- John Coffin, Tufts University
- Ronald Desrosiers, Harvard Medical School
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- Beatrice Hahn, University of Alabama, Birmingham
- Scott Hammer, Columbia Presbyterian Medical Center
- George Shaw, University of Alabama, Birmingham
- Joseph Sodroski, Dana-Farber Cancer Institute, Harvard Medical School

Progress to Date

- View the Annual and Interim Progress Report Summaries
- View Publications