Montefiori: Antibody Vaccine Immune Monitoring Consortium

OVERVIEW

The Comprehensive Antibody Vaccine Immune Monitoring Consortium (CAVIMC) utilizes valid laboratory criteria and Good Clinical Laboratory Practices (GCLP) to monitor systemic and mucosal antibodies in preclinical and clinical testing of candidate HIV vaccines and passively delivered antibodies. We also seek to identify correlates of protective immunity and to generate new scientific findings that will help bridge the gap between preclinical research and human clinical trials. These combined efforts aim to facilitate the discovery and licensure of a safe, effective and practical HIV vaccine, or long-acting pharmacologic intervention, to reduce the acquisition of HIV infection.

RESEARCH OBJECTIVES

1.) Obtain increased knowledge of potential immune correlates from active immunization strategies to guide the design and identification of an effective HIV vaccine.

2.) Obtain increased knowledge of potential immune correlates from passive immunization strategies to guide the design and identification of effective long-acting pharmacologic interventions to reduce the acquisition of HIV infection.

3.) Obtain enhanced understanding of what antibody activities to measure and how best to measure them to obtain valid results through development and improvement in reagents and assay protocols.

4.) Obtain new scientific findings to help bridge the gap between preclinical vaccine discovery and human clinical trials.

5.) Assure best in class assay services and reagents in order to satisfy external regulatory agencies.

6.) Facilitate collaboration and integration of the consortium within the CAVD, ensure effective and efficient operation of consortium and provision of CSF services, and the ability to quickly adapt to the changing needs of the CAVD.

PROGRESS

- The CAVIMC offers best in class assays for assessing neutralization, antigen binding, ADCC, phagocytosis, infecting cell binding, FcR binding and IgG glycan profiles in preclinical and clinical studies as part of their Central Service Facility. Antibodies are assessed in terms of their magnitude, breadth, kinetics, durability, epitope specificities, isotype/subclass and affinity/avidity.

- The CAVIMC provides customized, quantitative binding and neutralization measures of serum bnAb concentrations for pharmacokinetic (PK) assessments of passively transferred bnAbs. The CAVIMC also provides measurements of anti-drug antibodies (ADA) in preclinical and clinical studies of passive bnAbs.

- The CAVIMC provides critical assay support for bnAb optimization for manufacturability, GMP product stability and extended plasma half-life of engineered bnAbs for clinical development.

- The CAVIMC tailors new qualified assays to meet the evolving needs of the CAVD.

- The CAVIMC maintains a strong Central Quality Assurance Unit that oversees all quality aspects of Good Clinical Laboratory Practice (GCLP) compliant CAVIMC Cores and enables them to provide best in class assay services and reagents.

- The CAVIMC has developed novel reagents and approaches to enable monitoring of the earliest stages of bnAb induction in preclinical and clinical studies.

- The CAVIMC provides detailed characterization of neutralizing antibody responses induced by a wide range of engineered envelope immunogens, including different SOSIP configurations and adjuvants

- The CAVIMC continues to develop new computational methods and conduct analyses. The CAVIMC acquired a deeper understanding of which bnAbs and their combinations are most favorable for clinical development based on an expanded analysis of recent bnAbs, bispecific bnAbs and a wider range of viral subtypes.

- The CAVIMC evaluates and identifies non-neutralizing antibody correlates of protection against SHIV challenge in nonhuman primates.

- The CAVIMC maintains a strong program in molecular virology needed to overcome the genetic variability of HIV-1 as a barrier to vaccine discovery.

- The CAVIMC developed a novel assay approach to generate env quasispecies viruses of infectious molecular clones (Env.QS-IMC) from HIV-infected subjects for rapidly testing their neutralization sensitivity to bnAbs being passively infused and virus escape studies.

Grant at a Glance

Principal Investigator
David Montefiori, PhD

Grantee Institution
Duke University, Durham, USA

Project Title
Comprehensive Antibody Vaccine Immune Monitoring Consortium

OPPID
1146996

Grant Award
Up to $33.8 Million, awarded June, 2006
Up to $32.4 Million, awarded June 2011
Up to $32.6 million, awarded July 2016

Collaborating Institutions
- Beth Israel Deaconess Medical Center, USA
- Fraunhofer – Institut fur Biomedizinische Technik, Germany
- Massachusetts General Hospital, USA
- National Institute for Communicable Diseases, South Africa
- New Mexico Consortium, USA
- Thayer School of Engineering at Dartmouth
- University of Alabama at Birmingham, USA
- University of Cape Town, South Africa

External Scientific Advisory Board
- James Hoxie, University of Pennsylvania (Chair)
- Patricia D'Souza, National Institutes of Allergy and Infectious Diseases
- Shiu-Lok Hu, University of Washington
- Quentin Sattentau, The Sir William Dunn School of Pathology