Global NEUT Workshop
Varese, Italy, 17-18 March 2007

Development of immunological platforms in support of vaccine trials

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The Need for a Global HIV Vaccine Enterprise


June 27, 2003
Developed through a process of consultation involving more than 140 scientists from 17 countries
Scientific Priorities of the Enterprise Plan

**Vaccine Discovery**
- Characterization of recently transmitted virus
  - Immune correlates in primate models
  - Design of antibody-inducing vaccines
  - Design of T-cell-inducing vaccines

**Laboratory standardization**
- Standardization of current assays (antibodies and cell-mediated)
- Development of novel assays
- Development, production and distribution of reagents
  - Quality Assurance

**Product development and manufacturing**
- Bioprocess and analytical development group(s)
  - Manufacturing facility(es)

**Clinical trials capacity**
- Training of research staff
  - Development of sustainable facilities to support trials
  - Expanding access to trial populations

**Regulatory issues**
- Harmonization of regulatory requirements
  - Facilitation of decision making
  - Risk-benefit assessment in decision making
  - Strengthening of regulatory capacity in developing countries
  - Ethical issues

**Intellectual Property**
- Minimize restrictions on “freedom to operate”
  - Sharing of information
  - Recognition of contribution of partners
  - Maximize access to technologies and inventions
Collaboration for AIDS Vaccine Discovery

- 11 Vaccine Discovery Consortia (VDC)
  - 5 focused on neutralizing antibodies
  - 6 focused on cell mediated immunity
- 5 Central Service Facilities
  - 2 Vaccine immune Monitoring Centers
  - 1 Mouse Immunology Lab
  - 1 Specimen repository
  - 1 Statistical Center
Original CAVD Network Map

VDAC
VIMC
VDTC
Central Facilities
Intermediaries
Others

Neil Abernethy

the collaboration for AIDS vaccine discovery
A Global Network of Researchers

- CAVD PI Sites

- Countries with Researchers

Canada
United States
United Kingdom
Sweden
The Netherlands
Denmark
Germany
Austria
Belgium
France
Switzerland
Spain
Cameroon
Uganda
South Africa
Brazil
Zambia
Japan
China
Australia
Thailand
India
South Africa
United States
United Kingdom
Sweden
Cameroon
Comprehensive Antibody – Vaccine Immune Monitoring Consortium (CA-VIMC)

28 co-investigators, 19 institutions worldwide
Project Objectives and Goals

- Establish valid laboratory criteria to judge candidate vaccine immunogens based on antibody responses in preclinical and clinical stages of development.

- Speed the development of an effective vaccine by contributing key reference reagents, validated assays, shared SOPs, new assay technologies, increased laboratory capacity and quality assurance oversight.

- Adhere to GCLP requirements for human clinical trials to facilitate the licensure and timely access of approved products.

- Engage scientists from developing countries with the goal of facilitating international vaccine trials and enabling new scientific initiatives that will lead to more rapid vaccine discovery (Africa, India, China, Thailand, S. America).
Components

- Immune Monitoring Services – Core and Regional Laboratories
- Standard Virus Panel Consortium (SVPC)
- Neutralization Serotype Discovery Program (NSDP)
- Acute Infection Specimen Acquisition Laboratory (AISAL)
- Reference Laboratory (RL)
- Quality Assurance Unit (QAU)
- Research & Development (R&D)
- Sequence Analysis Center (LANL)
- Vaccine Immunology Statistical Center (VISC)
Immune Monitoring Services

Assist the CAVD Vaccine Discovery Groups (VDCs) and other groups in need by providing reliable measurements of vaccine-elicited antibody responses that will help identify improved vaccine immunogens.

- Preclinical NAb Core – Harvard
- GCLP NAb Core – NVITAL
- GCLP ELISA Core – Duke
- GCLP ADCC Core – Duke

Regional Laboratories

- Demonstrate competency and proficiency in assay performance (neutralization, ELISA, other).
- Perform ancillary studies related to assay and reagent standardization, including participation in SVPC and NSDP.
- Monitor vaccine-elicited neutralizing Ab responses in preclinical and clinical trials.
Reference Laboratory – Duke

Overall success of the CA-VIMC will depend on a rigorous program of assay standardization, validation, SOP development, interactive training and regular competency and proficiency testing in preclinical and clinical laboratories.

Quality Assurance Unit – Duke

The CA-VIMC will implement and supervise policies regarding common topics of quality assurance for laboratories that perform end-point assays on specimens from human clinical trials.
Cloning/Sequencing Centers

Functional gp160 clones from a large number of diverse HIV-1 strains need to be generated and sequenced to assure the success of the standard virus panel consortium (SVPC) and neutralization serotype discovery program (NSDP). In addition, full genome sequencing of these same virus strains will facilitate the development of standardized reagents for T cell assays.

Acute Infection Specimen Acquisition Laboratory – Harvard

Acquire plasma, sera and PBMC from early seroconverters at diverse geographic locations, including international vaccine trial sites, for Env cloning, full genome sequencing and new monoclonal Abs.
Research & Development

Develop new assays and monoclonal antibodies to provide a better understanding of vaccine-elicited antibodies. Focus on neutralizing antibodies and other potentially protective antibodies, including but not limited to ADCC and antibodies in the mucosal compartment.

Sequence Database

This will be the first large-scale effort to generate neutralization data with viral reagents that have a precisely known Env sequence. This information may be used to identify genetic signatures of neutralization phenotypes, to delineate neutralization serotypes, and to identify optimal peptide reagents for T cell assays.
Vaccine Immunology Statistical Center (VISC)

The CA-VIMC will work closely with the VISC to:

- design and implement an efficient system to capture, manage and analyze specimen information and antibody data from preclinical and clinical vaccine studies
- perform biostatistical analyses of data from assay validation experiments, proficiency testing and for reference reagent development
Global HIV Vaccine Research Cryorepository – GHRC

- HIV specimen collection
  - Clinical samples: plasma, PBMC, virus isolates
  - Key reagents from CAVD consortia: vectors, candidate vaccines, peptides, antibodies, rec. proteins
- New strategies of sample collection (e.g. “early infections”).
- New quality of preservation technology and sample processing.
- Future-proof technology for collecting, preparing, conserving and distributing reagents for extended networks.
- Technology upgrade of primary sites and transfer of operating procedures to and exchange of specimens with other VIMCs and VDCs.
CAVD Data and Materials Transfer

- Provide a menu of materials and reagents available for CAVD studies
  - Background information
  - Contacts
- Providing a database of record for tracking CAVD MTAs and CDAs
- Review the volume of material and data transferred between CAVD members with the Council of PIs
I. **Intra-VDC and Intra-CSF studies**
   a. According to individual VDC and CSF agreements
   b. Team sites on CAVD Portal
   c. Encouraged to share data and materials with CAVD members

**Abbreviations**
- **CSFs** = Central Service Facilities
- **VDCs** = Vaccine Discovery Consortia
- **VIMC** = Vaccine Immunology Monitoring Center
- **VISD** = Vaccine Immunology Statistical Center
- **HSC** = HIV Specimen Cryorepository
II. Non-Standardized Exchange Among CAVD Members
   a. According to CAVD Universal Agreement (VDC-VDC, CSF-CSF, VDC-CSF)
   b. Use of CSFs by VDCs
      a. Biostatistical Consultancy with VISC
      b. Lab science consultation with CA-VIMC, CT-VIMC, or MIL
      c. Custom transgenic mouse experiments
      d. Encouraged to deposit materials/reagents in HSC
   c. Transfers to and from VDCs and CSFs with CAVD Record Forms
   d. Encouraged to share data and materials with CAVD members
III. Standardized Evaluation of Vaccines

a. According to CAVD Universal Agreement (VDC-CSF)
b. Registration of studies with VISC (mouse, NHP, Clinical)
c. Use of Standardized Assays
d. Transfers with Record Forms and treatment of data
   1. According to Guiding Principles
   2. VDC release data to CAVD members and encouraged to use HSC
## CAVD Topics (wiki enabled)

### Vaccine Discovery Topics
- Immunogens/Inserts
- Adjuvants
- Carriers/Vectors
- Vehicles
- Route and delivery
- Animal models
- Challenge viruses
- Assays

### Preclinical Development Topics
- Fermentation and Cell Culture
- Purification
- Biophysical Research
- Vaccine Formulation
- GMP Compliance
- Safety Assessment
- Regulatory Documentation

### General Topics
- Guiding Principles
- Material Transfer Agreements
- Non-Disclosure Agreements