AIDS VACCINE DESIGN AND DEVELOPMENT LABORATORY

Building a New Vision in AIDS Vaccine Discovery
THE AIDS PANDEMIC, already among the most devastating in medical history, shows little sign of abating. Today, an estimated 33 million people are living with HIV. Some 7,500 others become infected with the virus every day. While programs to prevent HIV transmission using existing methods have saved countless lives, it has long been clear that nothing could stem the tide of new infections as effectively as a vaccine.

In keeping with its mission to ensure the development of a preventive AIDS vaccine that is safe, effective and accessible to everyone, the nonprofit International AIDS Vaccine Initiative (IAVI) is proud to announce the establishment of a new state-of-the-art applied research facility in New York City, the AIDS Vaccine Design and Development Laboratory. The Design Lab is the only facility in the world dedicated exclusively to the development of an AIDS vaccine. Together with partners in academia, the private sector and government, the lab is poised to conceive, compare, prioritize and advance promising AIDS-vaccine strategies, with the ultimate goal of ending the AIDS pandemic through an effective vaccine.

Specifically, the Design Lab’s programs aim to:

- create immunogens that will prompt the immune system to produce antibodies that neutralize the diverse types of HIV circulating worldwide today;

- design and prioritize viral vector-based AIDS vaccine candidates more effective than those in the current pipeline;

- uncover vital clues about how to design a human AIDS vaccine by studying a model found to be effective in non-human primates.

Over time, it has become clear that developing an AIDS vaccine will require more than testing existing vaccine concepts in clinical trials. There must also be a renewed focus on understanding the molecular details of HIV infection and the immune system’s response to the virus. Such applied research will help scientists devise new vaccine strategies to defeat HIV.
Who will do this work? Academic researchers working alone brim with inspiration but rarely have sufficient funds, infrastructure or industrial experience to advance a candidate vaccine into clinical studies. Private-sector manufacturers possess those resources but, because of the scientific challenges and the attendant risk that any single AIDS vaccine venture will fail, lack a strong profit incentive. That is especially true given that the market for an AIDS vaccine is principally in the developing world.

Addressing this gap is one of the goals of IAVI’s global AIDS vaccine discovery network, with the Design Lab as its latest addition. No one company, organization or country has the resources, know-how or capacity to design, develop and test an AIDS vaccine. Thus the Design Lab, like IAVI’s other programs, will work with a myriad of partners – in academia, industry, government and the non-profit sector. Together they will collaborate to identify and advance ideas with potential, from the lab bench to manufacturing through clinical trials.

As a nonprofit, IAVI can help move forward promising concepts wherever they originate. As a public-private partnership, it does so using private-sector methods to fulfill public-sector goals. The Design Lab’s scientists, with external partners, will explore innovative ideas from academia, basic research and beyond, using the tried and true methods of industry to speed the development of a public good: an AIDS vaccine for use throughout the world.

The Design Lab’s central purpose is to support the early development of novel and promising AIDS vaccine concepts, without duplicating work being done elsewhere. Much of the research at the lab will be integrated with work conducted by IAVI-organized scientific consortia that connect some of the world’s leading laboratories working on AIDS vaccine discovery. To ensure
businesslike efficiency, IAVI has modeled the lab on the blueprint of a typical commercial laboratory. Many of the scientists enlisted to work in the Design Lab gained their experience in vaccine discovery and development in the pharmaceutical sector and are adept at project and portfolio management.

The efforts of the Design Lab will produce new AIDS vaccine candidates to complement those already being developed through IAVI’s partnerships with external companies. Candidate vaccines emerging from the Design Lab will be tested in the network of clinical research centers IAVI and partners established and support in the developing world, where the AIDS epidemic is most acute.

As a global city, New York is a natural home for the Design Lab. The city has the highest concentration of academic institutions in the world and is home to more than 125 bioscience companies and nine world-class medical centers. Among the lab’s affiliates is the State University of New York’s Downstate Medical Center, where IAVI’s discovery facility was originally incubated. Through partnerships with laboratories overseas and training initiatives for investigators in developing countries, the lab will help build science capacity worldwide and train the next generation of AIDS vaccine specialists.

The scientists supported by IAVI are able to pursue their exciting work only because generous donors share our commitment to ending the AIDS pandemic by developing a vaccine. Few challenges today are more urgent or compelling. And few endeavors offer greater potential reward. We invite you to be a part of this venture and to visit our new laboratory in New York City. We think you’ll be inspired.
### NEUTRALIZING ANTIBODY CONSORTIUM (NAC)

<table>
<thead>
<tr>
<th>Institution</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indian Institute of Science</td>
<td>Bangalore, India</td>
</tr>
<tr>
<td>International Center for Genetic Engineering and Biotechnology</td>
<td>New Delhi, India</td>
</tr>
<tr>
<td>Karolinska Institute</td>
<td>Stockholm, Sweden</td>
</tr>
<tr>
<td>Institute for Research in Biomedicine</td>
<td>Bellinzona, Switzerland</td>
</tr>
<tr>
<td>Academia Sinica</td>
<td>Taipei, Taiwan</td>
</tr>
<tr>
<td>Mahidol University-Henry Jackson Foundation</td>
<td>Bangkok, Thailand</td>
</tr>
<tr>
<td>St. Stephen’s AIDS Trust</td>
<td>London, UK</td>
</tr>
<tr>
<td>University of Oxford</td>
<td>Oxford, UK</td>
</tr>
<tr>
<td>Vaccine Research Center, National Institute of Allergy &amp; Infectious Disease</td>
<td>Bethesda, MD, USA</td>
</tr>
<tr>
<td>Dana-Farber Cancer Institute</td>
<td>Boston, MA, USA</td>
</tr>
<tr>
<td>Harvard Medical School</td>
<td>Cambridge, MA, USA</td>
</tr>
<tr>
<td>The Scripps Research Institute</td>
<td>La Jolla, CA, USA</td>
</tr>
<tr>
<td>University of Wisconsin-Madison</td>
<td>Madison, WI, USA</td>
</tr>
<tr>
<td>International AIDS Vaccine Initiative</td>
<td>New York City, NY, USA</td>
</tr>
<tr>
<td>Children’s Hospital of Philadelphia</td>
<td>Philadelphia, PA, USA</td>
</tr>
<tr>
<td>University of Pennsylvania</td>
<td>Philadelphia, PA, USA</td>
</tr>
<tr>
<td>University of Washington</td>
<td>Seattle, WA, USA</td>
</tr>
</tbody>
</table>

### VECTORS CONSORTIUM (VEC)

<table>
<thead>
<tr>
<th>Institution</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Cancer Institute</td>
<td>Bethesda, MD, USA</td>
</tr>
<tr>
<td>Harvard Medical School</td>
<td>Cambridge, MA, USA</td>
</tr>
<tr>
<td>New England Primate Research Center</td>
<td>Cambridge, MA, USA</td>
</tr>
<tr>
<td>Global Vaccine Inc.</td>
<td>Chapel Hill, NC, USA</td>
</tr>
<tr>
<td>Cincinnati Children’s Hospital Medical Center</td>
<td>Cincinnati, OH, USA</td>
</tr>
<tr>
<td>The Scripps Research Institute</td>
<td>La Jolla, CA, USA</td>
</tr>
<tr>
<td>University of Wisconsin-Madison</td>
<td>Madison, WI, USA</td>
</tr>
<tr>
<td>International AIDS Vaccine Initiative</td>
<td>New York City, NY, USA</td>
</tr>
<tr>
<td>Children’s Hospital of Philadelphia</td>
<td>Philadelphia, PA, USA</td>
</tr>
<tr>
<td>Oregon Health &amp; Science University</td>
<td>Portland, OR, USA</td>
</tr>
</tbody>
</table>
Vaccines work essentially by “teaching” the immune system to recognize an invading pathogen and destroy it before it can cause disease. The vaccines that are most effective against viruses work by activating both cell-mediated immunity, which targets and destroys human cells already infected with viruses, and the antibody response, which takes out viruses that haven’t yet slipped into cells. The Design Lab’s three programs will focus on both of these arms of the immune system.

**The Immunogen Design Program**

This program focuses on creating immunogens that will train the immune system to recognize a unique protein (or antigen) on HIV’s surface. This, in turn, will equip the body to battle HIV if it encounters the virus. The program:

- discovers and analyzes rare antibodies capable of destroying HIV, in close coordination with the global IAVI-sponsored Neutralizing Antibody Consortium, which has recently opened a major new center at the Scripps Research Institute in La Jolla, California;
- uses knowledge of HIV’s vulnerabilities to create conceptually unique prototype vaccines;
- harnesses medicinal chemistry – rather than the genetic- and protein-engineering technologies typically used to generate immunogens – to create synthetic replicas of HIV’s vulnerable spots, in collaboration with research teams in India;
- conducts animal studies to assess the ability of novel immunogens to evoke neutralizing antibody responses.

HIV’s surface protein, called Envelope, is the major target for antibodies against HIV and thus the focus of the lab’s Immunogen Design Program.
Most AIDS vaccine candidates are constructed by inserting genes that encode HIV antigens into a harmless, unrelated, modified virus. Unlike their naturally occurring counterparts, these viral "vectors" are engineered to be incapable of replicating. This may limit a vector's ability to provoke a strong immune response in parts of the body where immunity to HIV matters most. Researchers suspect that replicating vectors are more likely to colonize the tissues of the gut, where HIV lands and establishes a beachhead. By training specialized immune cells at these sites to recognize HIV, a vaccine delivered in such a vector could blunt HIV before the virus permanently seeds other parts of the body. The Vector Design and Process Development Program:

- develops safe vectors that retain the ability to replicate in the human body and thus behave more like naturally occurring viruses;

- employs process-development expertise to accelerate the translation of the most promising vaccine concepts into products that are ready for clinical testing.
The Preclinical Immunobiology Program

This program plays a vital role in coordinating and integrating IAVI’s preclinical vaccine-discovery initiatives. To fulfill this goal, the program:

- oversees the evaluation of novel immunogens and vectors in animal studies;
- develops, in collaboration with IAVI’s Human Immunology Lab in London, assays, or tests, to ensure that vaccine candidates are comparably assessed in preclinical studies and clinical trials;
- oversees the standardization of common laboratory methods, materials and assays – ensuring that data generated in different labs at different times can be meaningfully compared;
- serves as a lynchpin in IAVI’s Live Attenuated Consortium, which seeks to uncover clues to thwarting HIV infection in humans by studying the immunology of non-human primates that have been effectively immunized with vaccines based on weakened Simian Immunodeficiency Virus (SIV), a cousin to HIV. Live-attenuated SIV is the most effective vaccine strategy in preclinical models.

Learning From the Live-Attenuated Model

Live-attenuated vaccines use a weakened but live version of the targeted pathogen. Because of safety concerns, this is not an option for HIV. However, live-attenuated vaccines made from the related Simian Immunodeficiency Virus (SIV) offer researchers vital lessons. As the charts below show, non-human primates exposed to SIV get infected. The amount of SIV in their blood peaks, falls, then steadily rises. Eventually they develop AIDS. Non-human primates vaccinated with live-attenuated SIV before being exposed to the virus also get infected, but their viral peak is much lower, and it stays low, with no sign of illness. The challenge is to repeat this kind of protection in humans with an AIDS vaccine.
A Word of Thanks

We wish to thank the many generous donors who have supported IAVI’s work since the organization was founded, and who have made the establishment of the AIDS Vaccine Design and Development Laboratory possible. We are grateful to the New York City Economic Development Corporation for underwriting the construction costs of the laboratory, to the Bill & Melinda Gates Foundation for funding key aspects of the research conducted at the lab, and to The Starr Foundation for its major leadership support. We also acknowledge The New York Community Trust and the James B. Pendleton Charitable Trust for their early contributions to the laboratory’s establishment and to Becton Dickinson (BD) and Thermo Fisher Scientific for generous product donations. We promise that the beneficence of our supporters will be put to good use in the effort to bring an end to AIDS.

IAVI gratefully acknowledges the generous support provided by the following major donors.*

Alfred P. Sloan Foundation
Basque Autonomous Government
Becton, Dickinson and Company (BD)
Bill & Melinda Gates Foundation
Bristol-Myers Squibb (BMS)
Broadway Cares/Equity Fights AIDS
Canadian International Development Agency
The City of New York, Economic Development Corporation
Continental Airlines
European Union
Foundation for the National Institutes of Health
Google Inc.
The Haas Trusts
Henry Schein, Inc.
Irish Aid
James B. Pendleton Charitable Trust
The John D. Evans Foundation
Kathy Bole & Paul Klingenstein
Merck & Co., Inc.
Ministry of Foreign Affairs and Cooperation, Spain
Ministry of Foreign Affairs of Denmark
Ministry of Foreign Affairs of The Netherlands
Ministry of Foreign Affairs of Sweden
The New York Community Trust
Norwegian Royal Ministry of Foreign Affairs
Pfizer Inc.
The Rockefeller Foundation
The Starr Foundation
Swedish International Development Cooperation Agency
Thermo Fisher Scientific Inc.
U.K. Department for International Development
Until There’s a Cure Foundation
The U.S. President’s Emergency Plan for AIDS Relief through the U.S. Agency for International Development
The William and Flora Hewlett Foundation
The World Bank through its Development Grant Facility

* As of 10/08

And many other generous individuals from around the world.
IAVI's mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world.

For more information about AIDS vaccine development visit: www.iavi.org