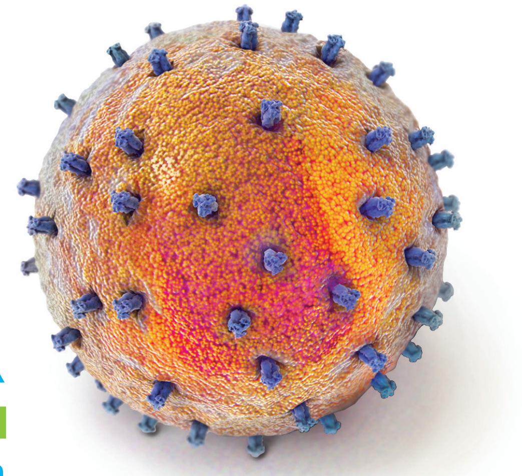
NOVEMBER 2012 | VOLUME 10 | NUMBER 5

vax

The Bulletin on AIDS Vaccine Research



[SPOTLIGHT]

Of Mice and Men

Will those hard-working humanized mice help get us to an AIDS vaccine? Scientists are sounding more optimistic. *By Regina McEnery*

It's difficult to imagine how an animal that fits in the palm of one's hand could be rejiggered to behave like Uncle Harry or Aunt Jo—or, more accurately, Uncle Harry or Aunt Jo with a raging viral infection. But some mice that have been genetically engineered to lack an immune system can do just that because they can accept almost any kind of transplant. This means that they can be made to carry functioning human genes, cells, tissues, and organs, and used to study human diseases in ways that would be ethically unacceptable or technically impossible in humans.

The first humanized mice were created more than two decades ago. Since then, substantial improvements have been made to their transplanted immune systems, improving their reliability as preclinical animal models. There are now four major types of humanized mouse models being used to study everything from diabetes and autoimmunity to cancer and a wide array of infectious diseases.

But no other infectious agent has been more extensively studied in humanized mice than HIV. Though primates are still considered the best model for studying HIV infection, humanized mice have the advantage of being far less costly. As their quality improves, they are becoming integral to HIV research. They have been used, for instance, to test new HIV drugs and the systemic delivery of neutralizing antibodies—highly specific proteins that bind viruses and prevent them from infecting host cells.

In recent years, scientists have designed humanized mice that appear to recapitulate a particularly troublesome aspect of HIV infection: the persistence of HIV in reservoirs of latently infected $CD4^+$ T cells—even after treatment has suppressed the virus to virtually undetectable levels in the blood. Such mice are likely to prove valuable to growing efforts to find a cure for HIV, which have lately focused on reactivating such latent reservoirs so that they can be targeted and destroyed.

Humanized mouse models have also long been sought to aid in the development of an AIDS vaccine. However, limitations in the ability of these models to develop functional T-cell responses against the virus that mimic those in humans—a critical arm of a vaccine-induced response to HIV—has tempered enthusiasm for these small animal models. Moreover, difficulties in infecting humanized mice through their mucosa due to the lack of sufficient human cells in the vaginal, rectal, and gastrointestinal tracts have similarly impeded efforts to use the mice to study HIV transmission and pathogenesis.

But a series of papers published this year suggests researchers have found a way around these barriers—most notably with the creation of the bone marrow-liver-thymus (BLT) humanized mouse. Those mice took a starring role at an all-day symposium at Harvard Medical School in Boston on Nov. 5 devoted to the application of humanized mouse models to AIDS vaccine development. "The immune responses in these models are very similar to what we see in human infection," said Todd Allen, co-chair of the symposium and principal investigator at The Ragon Institute of Massachusetts General Hospital (MGH), Massachusetts Institute of Technology (MIT), and Harvard. "But we don't know yet how well that will play out following vaccination of these mice. The biggest limitation is that this remains a model of a human immune system in a mouse environment."

A flurry of findings

Allen led a recent study that caused a small stir in AIDS vaccine research circles. He and his colleagues found that BLT mice infected with HIV mounted cellular immune responses that closely mirrored those observed in HIV-infected humans, and

NOTE TO SUBSCRIBERS

Starting next year, VAX will no longer be publishing a print edition. But the coverage and conversation will continue online at our new website, www.vaxreport.org, where we will provide more extensive and timely coverage of news that relates to AIDS vaccines. Please let us know what you think, and Happy Holidays.

moreover that HIV also escaped from those responses in a manner very similar to natural infection. Finally, Allen and his team found that BLT mice carrying a human immune-related gene associated with enhanced control of viral replication suppressed the virus in a way that was virtually identical to how humans who express that same gene control the virus. Allen said his lab is now looking at the potential to induce human HIV-specific immune responses in the humanized mice through vaccination.

Though mice are much smaller than people, they can shed light on how HIV makes its way around the body—as was vividly illustrated by Allen's Harvard colleague Thorsten Memel. He and his team recently tracked HIV-infected human T cells in the lymph node of a humanized mouse using a high-tech surveillance tool called intravital microscopy. This was the first time scientists have visualized the behavior of such cells in a live animal. The study found that HIV-infected T cells migrate robustly in lymph nodes. A small subset of these infected cells derive from either multiple cell fusions or through multiple adhesions to other $CD4^+$ T cells in the lymph node. These interactions resulted in the formation of long continuous membrane surfaces that increased the length of infected cells some ten-fold. The researchers suggest that all this may facilitate cell-to-cell transmission of the virus and promote widespread HIV dissemination.

In yet another study, scientists injected humanized mouse muscle cells with a modified viral vector optimized for the production of various broadly neutralizing antibodies (bNAbs)—those that target a broad range of HIV's many genetic variants. They found that the antibodies prevented infection even when the animals were challenged with high doses of HIV. Alex Balazs, a researcher in David Baltimore's lab at California Institute of Technology, where the experiments were conducted, said it remains to be seen whether the results seen in BLT mice can be replicated in humans. "History has shown us that humans don't behave like mice," said Balazs. "We have to be prepared for surprises."

Humanized mice are contributing to research on novel therapies as well. Rockefeller University scientist Michel Nussenzweig has been testing cocktails of potent bNAbs as a therapy in humanized mice infected with HIV. He and his team have found that giving a single bNAb or even as many as three did not produce durable results; the virus rebounded weeks after the antibody treatment ceased. But when they increased the number of bNAbs used, the virus had still not rebounded in seven of the eight mice after two months. Researchers suspect that the expanding arsenal of more potent antibodies might improve the chances of this strategy working and, if so, might provide an alternative to the daily grind of antiretroviral therapy.

The origins of BLT

The BLT mouse was initially developed by virologist Victor Garcia-Martinez, who is now at the University of North Carolina, in conjunction with a team at the University of Minnesota. Scientists make the mice by surgically implanting them with human organoids, which are fetal liver and thymic tissue that mimic organs—in this case organs that are essential to the development of immune cells. The mice are then irradiated and given transplants of stem cells taken from human fetal livers. These cells take up residence in the bone marrow, establishing a source for the human immune system borne by BLT mice. Mice altered this way were found to have a wide range of human immune cells in their peripheral blood; the cells also infiltrated tissues and organs in the lungs, GI tract, and liver, just as they would in the human body.

Garcia-Martinez and his team showed that these mice developed human T cells at a furious pace after being injected with the bacterial toxin that causes toxic shock syndrome, or Toxic 1—one sign that their immune systems were similar to that of humans. The researchers also measured the amount of time it took the mice to produce cytokines and found that it corresponded with the time taken to induce human inflammatory responses.

But the transplanted BLT immune system is not identical to a human's. One challenge, for example, is that antibody-producing cells, known as B lymphocytes, don't mature properly in the bodies of these mice. Dale Greiner, a University of Massachusetts scientist who has authored two reviews on the impact of humanized mouse models on the study of human disease, said this may be because the lymphoid organs in such mice are disorganized. It is in these organs that the immune responses are amplified and refined, especially those involving the production of neutralizing antibodies—which are these days a central focus of HIV vaccine research.

In humans, he said, all of the components are "where they need to be." In humanized mice, "it is like walking into a warehouse, where everything is scattered." Greiner says that the genetic engineering required to remove the immune system in these mice, so that it can be replaced by a human one, might inadvertently disrupt the genes required to "organize" their lymphatic system in an immunologically functional manner.

Still, researchers are optimistic about the future of humanized mice in AIDS vaccine research and appear to believe the BLT model, in particular, can be tweaked and improved to that end. "What I think would really catalyze the field," said Andrew Tager, a Harvard Medical School scientist who collaborated with Allen on his recent study, "is if there could be funding for a consortium to focus on making this a better model with an eye toward answering more questions about HIV. How can we make the immune responses of the model even better? Do we need to put more human genes in the mice? We have shown we are on track. The time is now." ■

MANAGING EDITOR
Kristen Jill Kresge

SENIOR SCIENCE WRITER
Andreas von Bubnoff, PhD

SCIENCE WRITER
Regina McEnery

SENIOR PRODUCTION MANAGER
Nicole Sender

FREE SUBSCRIPTIONS:

To obtain a FREE subscription to *VAX* by e-mail, change your subscription details, or receive multiple print copies of *VAX* to distribute and/or use in your programs, please go to www.iavireport.org and click on the Subscribe link.

vax

VAX is a bi-monthly bulletin from IAVI Report, the publication on AIDS vaccine research published by the International AIDS Vaccine Initiative (IAVI). It is currently available in English, Spanish, and Portuguese as a downloadable PDF file or an e-mail bulletin.

The International AIDS Vaccine Initiative (IAVI) is a global not-for-profit organization whose mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world. Founded in 1996, IAVI works with partners in 25 countries to research, design and develop AIDS vaccine candidates. In addition, IAVI conducts policy analyses and serves as an advocate for the AIDS vaccine field. For more information, see www.iavi.org.

iavi International AIDS Vaccine Initiative

GLOBAL NEWS *by Regina McEnery*

Malaria vaccine candidate less effective in infants

New findings from an ongoing Phase III malaria vaccine trial in Africa suggest that the candidate, RTS,S, reduces the incidence of clinical malaria and severe malaria by a modest 31.3% and 36.6%, respectively, among children 6-12 weeks of age. Published online on Nov. 9 in the *New England Journal of Medicine*, the results nonetheless find that the efficacy of RTS,S was less than that reported last year for older children enrolled in the same trial (see *VAX* Nov. 2011 *Spotlight* article, *A Shot at Fighting Malaria*). It also appears to be lower than previously reported in a smaller Phase II trial.

Mary Hamel, a medical epidemiologist at the US Centers for Disease Control and Prevention and a principal investigator at one of the trial's clinical research centers in Kisumu, Kenya, said researchers should gain some clarity when data from all the sites where the study was conducted are released in the next year or two. "We may find that by pooling the data across the 11 trial sites, differences in vaccine efficacy by malaria transmission intensity were masked," Hamel says. "Most malaria cases in this analysis were from areas of very high transmission. Efficacy in areas of low or moderate malaria transmission may be higher, consistent with the Phase II trial."

Developed and manufactured by GlaxoSmithKline (GSK) Biologicals, RTS,S contains a protein found on the surface of the *P. falciparum* sporozoite—the form of the parasite transmitted from mosquitoes to people—linked to hepatitis B vaccine antigen. It is formulated with AS01, an adjuvant manufactured by GSK.

The RTS,S candidate was co-administered with two licensed vaccines: a pentavalent vaccine against diphtheria, tetanus, pertussis, hepatitis B and *Hemophilus influenzae* type B, and a polio vaccine. Scientists suggest that the co-administration of the licensed vaccines—including the Hep B antigen, which was effectively delivered twice—may have compromised the immune response to the RTS,S candidate. Hamel adds that infants have immature immune systems that respond less vigorously to vaccination, and that their responses might have been further compromised by antibodies against the sporozoites passed down by their mothers. Lower vaccine efficacy could also be associated with higher-transmission regions, but that will only be known when the site-specific analysis is completed.

The fate of RTS,S remains unclear. The PATH Malaria Vaccine Initiative, which financed most of the research with a $200 million grant from the Bill & Melinda Gates Foundation, hasn't yet announced any decision. "The efficacy came back lower than we had hoped, but developing a vaccine against a parasite is a very hard thing to do," said Bill Gates in a statement on PATH's website. "The trial is continuing, and we look forward to getting more data to help determine whether and how to deploy this vaccine."

Dybul to lead The Global Fund

Mark Dybul, a medical doctor and immunologist who helped create and then led the President's Emergency Program for AIDS Relief (PEPFAR) for three years, will be heading up The Global Fund to Fight AIDS, Tuberculosis and Malaria in Geneva.

Dybul's appointment comes at a particularly rocky time for The Global Fund, a prolific fundraiser that has been grappling with both funding and management problems in recent years (see *The Global Fund's Uncertain Future*, *IAVI Report*, Jan.-Feb. 2012). Dybul replaces Michel Kazatchkine, who left the organization in early 2012, not long after The Global Fund's board of directors appointed international banker Gabriel Jaramillo to the newly created position of general manager and put him in charge of day-to-day operations.

Dybul was a staff clinician at the US National Institute of Allergy and Infectious Diseases when he joined a task force that led to the creation of PEPFAR in 2003. Since 2009, he has co-directed the Global Health Law Program at the O'Neill Institute for National and Global Health Law at Georgetown University.

Q&A WITH MITCHELL WARREN

VAX recently asked the executive director of the global HIV-prevention advocacy group AVAC what he thinks US President Barack Obama's second term likely means for the global AIDS agenda.

Has the outcome of the US election changed the dynamics of contentious budgetary talks in Washington?

I hope it changes something. It really comes down to [whether] the US government finds a solution to the fiscal cliff by January. It is an incredibly important issue. If the US government goes into sequestration [across-the-board automatic spending cuts] it would have a staggeringly bad effect on both global health, and research and development. In the case of PEPFAR [the US President's Emergency Program for AIDS Relief], many countries have already gone through caps on treatment slots because resources are thinner. If we saw significant cuts to foreign aid, there would be even fewer people in treatment.

Do you think this crisis can be averted?

My hope, and I tend to be an optimist, is that they all seem to get it. Obviously the current business-as-usual has to change. But while hard cuts have to be made, sequestration is the worst way to do it. Jobs would be lost, progress would be rolled back.

What role are AIDS advocates playing during these budget talks?

A lot of advocacy has to be around making sure people see what the impact of sequestration will be. And I think we also need to make sure we keep in view the long arc of what we are trying to accomplish, to show the hard-fought investments that have been made. It took a long time to create these programs. Once you turn the tap off, and have to lay people off and close down programs, to restart [those programs] even a year later is far more complicated.

It looks like the Affordable Care Act [ACA] is here to stay. How will it impact HIV services?

One of the best things [in the law] is that prevention is now part of the health care system and that means more access to HIV testing and preventive services. And more people will also have access to care. The challenge right now is: How do you implement [the ACA]? Many states are in a waiting situation.

PEPFAR is also up for reauthorization next year. Where does it stand?

We need to make sure [PEPFAR] is funded robustly. There is also a concept you are hearing more and more called country ownership. Countries will need to step up and own their [AIDS] programs.

For entire interview, go to www.vaxreport.org.

Understanding DNA Vaccines

What are the major challenges that AIDS researchers have faced in developing DNA vaccines and how are recent advances helping them overcome these challenges? ***By Regina McEnery***

Many common viral vaccines have been made by either killing a virus of interest or weakening it so that it doesn't cause disease. When people are immunized with such preparations, they mount an immune response that subsequently protects them from pathogenic strains of the targeted virus. Unfortunately, using a weakened or attenuated version of HIV to stimulate protective immunity remains off limits to developers of AIDS vaccines. HIV mutates very rapidly, changing its genetic makeup dramatically even within one infected individual. Researchers therefore worry that an attenuated HIV could mutate and regain its ability to cause disease. Using a killed version of HIV in a vaccine candidate, meanwhile, is impractical because it is difficult to prove that the virus is completely inactivated. Further, such vaccines have failed to protect monkeys against simian immunodeficiency virus (SIV, the monkey equivalent of HIV).

These concerns have led scientists to look for better and safer methods for creating AIDS vaccine candidates. One such alternative is DNA vaccination, in which genes from a pathogen of interest are injected into people to generate a protective immune response. Essentially, DNA HIV vaccines are composed of harmless pieces of HIV's own DNA that have been pasted into circular pieces of DNA known as plasmids, which infect bacteria in the wild and have long been used to express genes in laboratories.

After an engineered and purified DNA plasmid is injected into a person—usually with a gene gun into skin and muscle—it is passively taken up by cells. Those cells then use their own protein-making machinery to produce the HIV proteins encoded by the plasmid. This usually results in the activation of the cellular immune response, which targets virally infected cells. But DNA vaccines can also be engineered to elicit antibody responses, which can block the viral invasion of cells and have historically played a central role in vaccine immunization (see Feb. 2004 *Primer* on *Understanding the Immune System, Part 1* and Mar. 2004 *Primer* on *Understanding the Immune System, Part II*).

When DNA vaccination was first proposed in the early 1990s, the preclinical data seemed promising. Scientists had found that mice inoculated subcutaneously with genes encoding human growth hormone developed antibodies against that protein. Further, DNA vaccine candidates were even then relatively easy to make and stable at room temperature. Researchers were therefore attracted to this strategy. It meant that such vaccine candidates could be produced relatively rapidly and cheaply in large quantities and would, further, suit the needs of the developing world, where refrigeration capacity is often limited and transportation difficult.

But DNA vaccine candidates also presented some challenges. Most prominently, they triggered relatively weak immune responses because plasmids are not very efficiently taken up by cells. Producing stable forms of engineered plasmid DNA also proved to be harder and more expensive than researchers had expected. These setbacks dampened enthusiasm for DNA vaccines, not just against HIV but other pathogens as well. In fact, no DNA vaccine has yet been licensed to prevent a human disease.

New tools improve responses

In recent years, however, technological advances have revitalized the field of DNA vaccination. One new tool that has contributed to its resurgence is electroporation (EP), a vaccine delivery technology that induces temporary pores in the membranes of muscle or skin cells so that they can more easily take plasmids. Small hand-held EP devices these days often include a needle to inject the vaccine and thin wires that administer short electrical pulses during vaccine delivery.

Initially developed in the 1970s, EP has been refined and tested in a growing number of human studies since the early 1990s. In recent years, EP devices have been tweaked to cause less pain and deliver plasmids more efficiently, and continue to be tested in HIV vaccine trials.

Adjuvants, which stimulate the immune response to vaccines, are also being used to improve DNA-based vaccine candidates. Many licensed vaccines, such as the influenza vaccine, are formulated with chemical adjuvants. But as researchers' understanding of the immune system and its factors has grown in sophistication, entirely novel adjuvants and methods for their co-delivery are being tried out in clinical trials. Rather than just co-formulate their vaccine candidates with adjuvants, for example, AIDS vaccine developers have designed DNA plasmids to carry genes for proteins that are potent boosters of cellular immune responses. One such protein, Interleukin 12, is naturally produced by dendritic cells—which have long been known to play a central role in vaccine immunization. Clinical trials are now testing DNA vaccine candidates that are delivered via electroporation along with the gene for IL-12.

Researchers have also tweaked the plasmids used to make DNA vaccines so that human cells can express more of the HIV antigens they encode, and so trigger more robust immune responses. One way they do this is by including in the plasmids promotors—DNA sequences that initiate the reading of genes for protein production—that are more effective at driving gene expression.

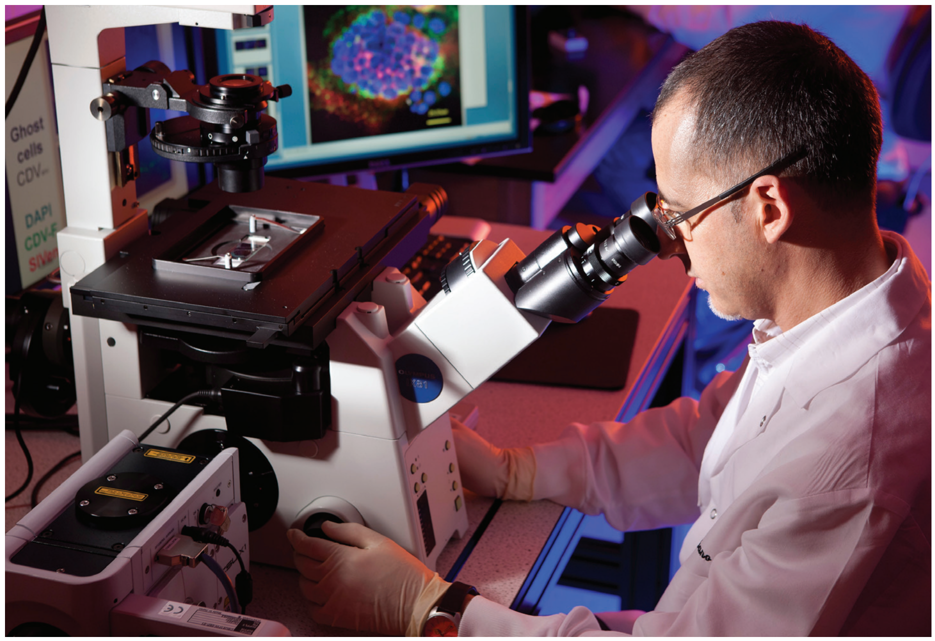
Vaccine developers also enhance immune responses by using DNA candidates as a prime, and then boosting the response it provokes with another agent—such as the canarypox viral-vector vaccine candidate that was used in the RV144 trial in Thailand. Any such regimen is referred to as a heterologous prime-boost. The DNA used as the prime focuses the immune response on the vaccine candidate inserts, perhaps with the help of an adjuvant. The subsequent boost enhances the primed response.

Together, new technologies and such traditional immunization strategies have contributed to a resurgence in DNA vaccine development. ■

JUNE 2012

About the International AIDS Vaccine Initiative

The International AIDS Vaccine Initiative (IAVI) is a global not-for-profit organization whose mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world. Founded in 1996, IAVI works with partners in 25 countries to research, design and develop AIDS vaccine candidates. In addition, IAVI conducts policy analyses and serves as an advocate for the AIDS vaccine field. IAVI supports a comprehensive approach to addressing HIV and AIDS that balances the expansion and strengthening of existing HIV-prevention and treatment programs with targeted investments in the design and development of new tools to prevent HIV. IAVI is also dedicated to ensuring that a future AIDS vaccine will be available and accessible to all who need it.



CHARLOTTE RAYMOND PHOTOGRAPHY/IAVI

RESEARCH AND DEVELOPMENT

Scientific partnerships are essential to the fulfillment of IAVI's mission. IAVI's scientific team, drawn largely from the vaccine industry, designs and develops HIV vaccine candidates and conducts HIV vaccine clinical trials and related epidemiological research in partnership with more than 50 academic, biotechnology, pharmaceutical and government institutions. The organization is advancing a portfolio of vaccine technologies and product candidates by prioritizing the most promising approaches, whether developed internally or by external parties. IAVI has devoted substantial resources to translational research to fill the role traditionally played by the biotechnology or biopharmaceutical industry.

IAVI also has brought together leading international HIV researchers spanning Asia, Europe and North America to form AIDS vaccine consortia to address major scientific problems in HIV vaccine development and boost the number and quality of novel vaccine candidates evaluated in clinical trials. To tackle one such scientific problem, the elicitation of antibodies that can neutralize a broad range of HIV variants, IAVI launched in 2002 the Neutralizing Antibody Consortium (NAC), and subsequently the IAVI Neutralizing Antibody Center at The Scripps Research Institute in La Jolla, California, which serves as the headquarters for the NAC. Since 2009, thanks in large measure to the efforts of the NAC, more than two dozen broadly neutralizing antibodies have been isolated from volunteers from around the world. These findings have made a significant impact on HIV vaccine research.

IAVI also conducts high-quality, integrated translational research at its AIDS Vaccine Design and Development

CHARLOTTE RAYMOND PHOTOGRAPHY/IAVI

research centers around the world, to inform vaccine design. These studies cover topics from basic questions of HIV epidemiology in potential trial populations to the cellular and molecular analysis of the immune system's response to HIV infection.

INNOVATION

IAVI's Innovation Fund harnesses early-stage technologies that have the potential to significantly advance AIDS vaccine development. Established in 2008 in collaboration with the Bill & Melinda Gates Foundation, the Innovation Fund is supporting short-term, high-risk, proof-of-concept studies on promising technologies' applicability to AIDS vaccine development. The recent isolation of two new broadly neutralizing HIV antibodies was enabled by an Innovation Fund recipient working with IAVI's scientists and a network of research centers around the world.

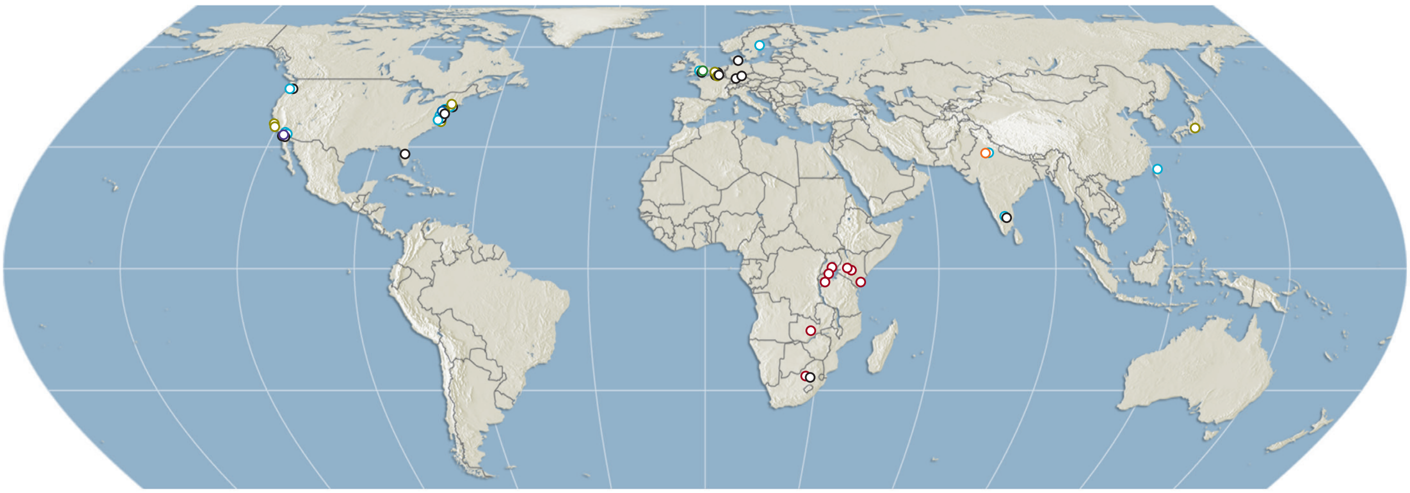
Laboratory (Design Lab) in New York City, and its Human Immunology Laboratory (HIL) in London, England. The Design Lab, established in 2008, connects IAV I's R&D efforts, linking design and development programs and providing scientific, material, logistical, technical and managerial support to our partners, other researchers and collaborating scientists. Based at Imperial College London, the HIL coordinates the IAV I-supported network of clinical trial centers. It trains and supports researchers and technicians, provides materials and quality assurance to the network, and plays a central role in generating the data that enables prioritization of vaccine candidates. The lab also is pioneering the development of standardized tests to improve the breadth, quality and detail of information researchers can collect on the interaction of HIV with the human immune system.

In addition, IAVI and the Translational Health Sciences and Technology Institute (THSTI) have agreed to jointly establish an HIV Vaccine Design Program in India that will include the establishment of a new center in the National Capital Region of New Delhi.

In the past 15 years, IAVI and its network of partners have developed and advanced 13 vaccine candidates into early-stage human trials in 11 countries in Asia, Africa, Europe and North America, conducted 15 observational epidemiological studies and provided voluntary testing and counseling to more than 235,000 individuals in Africa. IAVI network partners also have conducted clinical trials on other, non-vaccine HIV prevention technologies, including pre-exposure prophylaxis. Additionally, IAVI conducts non-interventional clinical research, in partnership with

PARTNERING WITH DEVELOPING COUNTRIES

IAVI recognized early on the importance of building partnerships and conducting vaccine trials in developing countries, where the need for a vaccine is greatest. Today, a network of independent but interconnected research centers in five sub-Saharan countries play a central role in IAVI's vaccine development program, testing HIV vaccine candidates and conducting epidemiological studies that inform the design of candidates and provide baseline information for future efficacy trials. Staffed with local scientists and clinicians and led largely by African HIV experts, these facilities are regional centers of excellence in HIV prevention research and are now leveraging IAVI-supported infrastructure to solicit funding for research related to a variety of other diseases.



IAVI and its partners also conduct educational initiatives, voluntary counseling and testing consultations, capacity building and training of research center staff to ensure the highest standards of ethics and quality in the clinical trial process. In this context, IAVI works to develop the physical infrastructure required for its research efforts, to ensure that volunteers clearly understand their rights and obligations as participants in clinical research through the informed-consent process, and to provide volunteers with access to high-quality medical services while participating in trials. The organization also supports local partners advocating for the creation of national AIDS vaccine development plans.

In other areas of the world where IAVI is not currently sponsoring AIDS vaccine trials—Brazil, China, India and Japan, for example—the organization works with on-the-ground partners to support national efforts in AIDS vaccine research and advocacy.

THE IAVI GLOBAL SCIENTIFIC NETWORK

Over the course of its history, IAVI has established a globe-spanning network of partnerships and facilities to accelerate the design, development and testing of AIDS vaccine candidates:

- **The AIDS Vaccine Design and Development Laboratory**
  New York, New York, US
- **The Human Immunology Laboratory**
  London, UK
- **The IAVI Neutralizing Antibody Center at The Scripps Research Institute**
  La Jolla, California, US
- **Centre for HIV Vaccine Design** (*under development*)
  New Delhi, India
- **IAVI-Supported Clinical Research Centers**
- **Neutralizing Antibody Consortium**
- **Innovation Fund Grant Recipients**
- **Corporate Vaccine Development Partners**

ADVOCACY & POLICY ANALYSIS

In collaboration with partner organizations, IAVI conducts policy analysis and advocacy to mobilize support for HIV vaccine research and development and prepare the ground for future access to such vaccines as an essential component of a comprehensive response to the HIV pandemic. Specifically, IAVI works with researchers, HIV prevention and treatment advocates, civil social organizations and communities most affected by the pandemic. IAVI also partners with allied groups and leaders working on global health issues, economic development and human rights to advocate for the full engagement of the developing world in efforts to prevent HIV and other endemic diseases.

In Europe, IAVI works closely with civil society partners at both the national and European Union level to cultivate political support and advocate for policy changes that support AIDS vaccine research. IAVI also collaborates with other product development partnerships (PDPs) to ensure that financing for AIDS vaccine research and development is included in EU research budgets, and to advocate for PDP funding lines in the legislation of individual European nations.

IAVI and its partners also aim to create a more supportive policy environment for HIV vaccine R&D at the global, regional and national levels—one that encourages innovation, collaboration and a sustained commitment of resources to all such efforts. In addition, IAVI publishes policy analyses on a wide range of topics, including annual funding levels for the development of new HIV prevention tools and the potential value and impact of HIV vaccines and other new HIV prevention technologies.

International AIDS Vaccine Initiative

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

Basque Autonomous Government (Spain) ■ Becton, Dickinson and Company (BD) ■ Bill & Melinda Gates Foundation ■ Bristol-Myers Squibb ■ Broadway Cares/Equity Fights AIDS ■ Canadian International Development Agency ■ The City of New York, Economic Development Corporation ■ Foundation for the National Institutes of Health ■ The Gilead Foundation ■ GlaxoSmithKline ■ Google Inc. ■ Government of Japan ■ The Hearst Foundations ■ Institut Mérieux ■ Irish Aid ■ James B. Pendleton Charitable Trust ■ Ministry of Foreign Affairs and Cooperation, Spain ■ Ministry of Foreign Affairs of Denmark ■ Ministry of Foreign Affairs of The Netherlands ■ Ministry of Science & Technology, Government of India ■ National Institute of Allergy and Infectious Diseases ■ Norwegian Royal Ministry of Foreign Affairs ■ The OPEC Fund for International Development ■ Pfizer Inc ■ The Starr Foundation ■ Swedish International Development Cooperation Agency ■ Thermo Fisher Scientific Inc. ■ U.K. Department for International Development ■ The U.S. President's Emergency Plan for AIDS Relief through the U.S. Agency for International Development ■ United Continental Airlines ■ The World Bank through its Development Grant Facility

And many other generous individuals from around the world

As of January 2012