

IAVI Report

The Publication on AIDS Vaccine Research

WWW.IAVIREPORT.ORG | VOLUME 23, ISSUE 1 | APRIL 2019

MDAMK
RGLCCVLLL
CGAVFVSPSQEIH
ARFRRGARAENLWVTVYYG VP
VWKDAETTLFCASDAKAYETEKH NVWATHACVP T
DPNPQEIHLNVTEEFNMWKNMVEQMHTDIISLW
DQSLKPCVKLTPLCVTLQCTNVTNNITDDMRGELKNCSF
NMTTEL**WITH NEW TRIALS UNDERWAY**DKKQKVYSLFYRL
DVVQINENQGNRSNNSNKEYRLINCNTSAITQACPKVSFEPIPIH
YCAPAGFAILKCKDKKFNGTGPCPSVSTVQCTHGIKPVVSTQLLNG
SLAEEEEVMIRSENITNNAKNILVQFNTPVQINCTRPNNNTRKSIRIGP
GQAFYATGDIIG **AND A SURGE OF OPTIMISM IN THE FIELD,** DIRQAH
CNVSKATWNETLGKVVKQLRKHFNGNTIIRFANSSGGDLEVTTHSFNCG
GEFFYCNTSGLFNSTWISNTSVQGSNSTGSNDSITLPCRIKQIINMWQRIG
QAMYAPPIQGVIRCVSNITGLILTRDGGSTNSTTETFRPGGGDMRDNRSEL
YKYKVVKIEPLGVAPTRCKRRVV **A NEW GENERATION** GRRRRRRAVIGIGAVF
LGFLGAAGSTMGAASMTLTVQARNLLSGIVQQSNLLRAEAQQHLLKLTVWG IKQL
QARVLAVERYLRDQQLLGIWGC SGKLIC **CTNVPWNSSWSNPRNLSEIWDNMTWLQW**
DKEISNYTQIIY GLLSEESQNNQEKNEQDLLALD*MDAMKRGLCCVLLL CGAV
FVSPSQ **OF AFRICAN SCIENTISTS** EIHARFRRGARA
ENLWVTVYYGVPVWKDAETTLFCASDAKAYETE
KHNWATHACVPTDPNPQEIHLNVTEEFNM
WKNMVEQMHTDIISLWDQSLKPCVKLTP
LCVTLQC **IS CONTRIBUTING** TNVTNNITD
DMRGELKNCSFNMTTEL RDKKQKVYS
LFYRLDVVQINENQGNRSNNSNKE
YRLINCNTSAITQACPKVSFEPIPI
HYCA **MORE THAN EVER** PAGFAIL
KCKDKKFNGTGPCPSVSTVQCTH
GIKPVVSTQLLNGSLAEEEEVMIRS
ENITNNAKNILVQFNTPVQINCTRP
NNNTRK **TO THE HUNT** SIRIGPGQAF
YATGDIIGDIRQAH CNVSKATWNET
LGKVVKQLRKHFNGNTIIRFAN
SSGGDLEVTTHSFNCGGEF
FYCN **FOR A VACCINE.** TSG
LFNSTWISNTSVQGSNST
GSNDSITLPCRIKQIIN
MWQRIGQAMYAPPIQ
GVIRCVSNITGLILT
RDGGSTNSTTE
TFRPGGGDM
RDNWRSE

Learn about the breakthrough behind these letters, page 9.

**A special issue
on HIV vaccine science
in Africa, for Africa**

FROM THE EDITOR

In 2007, I was in Cape Town to attend a symposium on the challenges of global vaccine development. At that meeting, and during my visits to nearby clinical research centers, the mood was somber.

Just weeks before, two HIV vaccine efficacy trials, known as STEP and Phambili, had ground to a halt. These trials were testing two variations of a viral vector-based vaccine candidate, developed by the pharmaceutical company Merck, which were largely viewed as among the most promising in development at the time. They were stopped mid-course for futility. Subsequent data suggested the vaccine candidate may have even enhanced the risk of HIV infection in a specific subset of volunteers. I interviewed dozens of researchers at that time, including IAVI's President and CEO Mark Feinberg, who was then with Merck. One of the dominant sentiments was that the field needed to go back to the drawing board.

Fast forward 12 years and there is an unbridled sense of optimism in the HIV prevention field, primarily due to scientific progress. There are now two vaccine efficacy trials and an efficacy study of antibodies for HIV prevention ongoing, all of them in Africa. There is also a new generation of HIV vaccine candidates entering clinical trials. These candidates harness the tremendous insights into natural infection and the development of broadly neutralizing antibodies that have been garnered during the last decade.

There is also significant progress on another front—the increasingly prominent role African scientists are playing in the quest to develop an HIV vaccine. Much of this progress is the result of a sustained effort by IAVI, through its decades-long partnership with the U.S. Agency for International Development (USAID), to nurture scientific talent on the African continent. This is the focus of IAVI's ADVANCE (Accelerate the Development of Vaccines and New Technologies to Combat the AIDS Epidemic) program, a five-year cooperative agreement between IAVI and USAID through the U.S. President's

Emergency Plan for AIDS Relief, which is investing in African-led HIV prevention research. That is the theme of this issue.

It is the first issue of IAVI Report we've ever dedicated to a single topic, and it is an important one. Margaret McCluskey, senior technical advisor for HIV vaccines at USAID, and her USAID colleagues Benny Kottiri and Samantha Luffy, wrote this in a recent email: "Upon recent site visits to the clinics and labs in East and Southern Africa, we have been deeply inspired by the elegant science being produced by the young scientists and their dedicated mentors. Thank you for considering our request to dedicate a special edition of IAVI Report to the extraordinary scientific capacity being built under ADVANCE."

To glimpse this, I attended a recent ADVANCE meeting in Lusaka, Zambia. What I heard at this meeting was that a notable transformation is underway. Not only is the mood more ebullient today, there is a cadre of passionate and talented young and mid-career African scientists who are contributing to HIV vaccine development more substantially than ever before. Some of their research is featured in this issue (see pages 10–16).

When I visited the Zambia Emory HIV Research Project (ZEHRP) clinical research center in Lusaka and sat in the reception area with more than a dozen women enrolled in the ongoing HVTN 705 vaccine efficacy trial, I was reminded of the necessity of an HIV vaccine. It isn't just about overcoming scientific obstacles or altering the statistics; it is about these young women and others like them. It is about striving to someday give them a long-lasting, affordable, non-stigmatizing vaccine that can protect them from HIV infection. It is about finding a way to make it possible that their children, some of whom were strapped to their backs at the clinic that day, can live in an AIDS-free world.

Today, more scientists in the countries most affected by HIV/AIDS are working to make that possible. That should inspire optimism too.

—Kristen Jill Kresge

IN THIS SPECIAL ISSUE

4 'We're moving in the right direction'
A conversation with Anatoli Kamali and Penny Moore about the rise of HIV vaccine science in Africa.

8 The best is yet to come
Africa is contributing far more than samples to scientific research. The continent's scientists are actively engaged in developing and testing novel HIV vaccine candidates.

Plus spotlights on four HIV researchers in Africa:

10 | Eunice Nduati

12 | Eugene Ruzagira

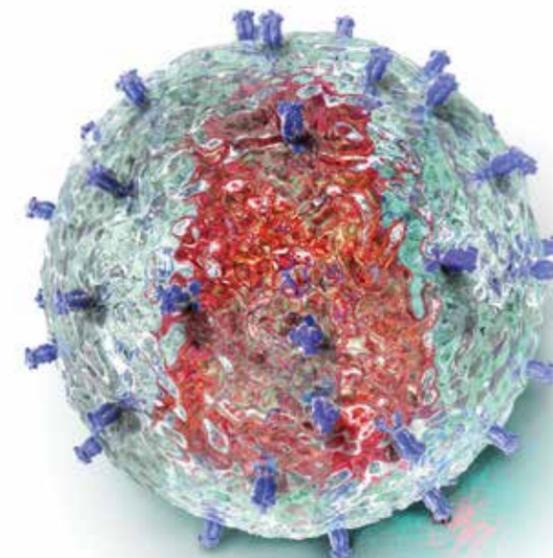
14 | Clive Michelo

16 | Sheila Balinda

22 Stopping HIV where it starts
Marianne Mureithi is part of a team of researchers that just received highly competitive funding to study mucosal immune responses to HIV in Kenya.

26 Upcoming trial illustrates the value of African-led science
Commentary: We must continue to engage local investigators and develop their capacity to conduct more basic and clinical research on the African continent.

And while you're thinking of us ...
Please take a few minutes to complete a survey on IAVI Report at <https://www.surveymonkey.com/r/WWL3JKY>



IAVIReport

ASSOCIATE DIRECTOR

Nicole Sender

MANAGING EDITOR

Kristen Jill Kresge

CONTRIBUTING WRITERS

Michael Dumiak

Karie Youngdahl

GRAPHIC DESIGNER

Jackson Dykman

Comments/questions?
iavireport@iavi.org



ON THE COVER

The cover image depicts the amino acid sequence of the BG505 SOSIP.664 protein, a native-like trimer that is currently being tested as an HIV vaccine candidate in the IAVI W001 trial in the U.S. and Kenya (see page 8). The protein was based on the BG505 HIV sequence isolated from a Kenyan infant (*J. Virol.* **80**, 835, 2006). The amino acids in bold signify those that were altered from this wild-type BG505 sequence to develop the stabilized, trimeric BG505 SOSIP.664 protein. Amino acid sequence printed with permission by Rogier Sanders at the Amsterdam University Medical Center (*PLoS Pathog.* **9**(9): e1003618, 2013).



All rights reserved ©2019

IAVI is a nonprofit scientific research organization dedicated to addressing urgent, unmet global health challenges including HIV and tuberculosis. Our mission is to translate scientific discoveries into affordable, accessible public health solutions to help the people who need them most. For more information, see www.iavi.org.

‘We’re moving in the right direction’

A conversation with Anatoli Kamali and Penny Moore about the rise of HIV vaccine science in Africa

BY KRISTEN JILL KRESGE

On a cloudy and cool evening in Lusaka in early February, I sat on an outdoor terrace talking with Anatoli Kamali and Penny Moore. The pair are witnessing first hand, though from different vantage points, the increasingly prominent role researchers and investigators in Africa are playing in the quest to develop an HIV vaccine.

Kamali is head of IAVI’s regional programs in Africa, and Moore is South African research chair of virus-host dynamics at the University of the Witwatersrand and the National Institute for Communicable Diseases. They were in the now verdant capital of Zambia for meetings on ADVANCE—Accelerate the Development of Vaccines and New Technologies to Combat the AIDS Epidemic—I AVI’s five-year program funded by the U.S. Agency for International Development (USAID), through the United States President’s Emergency Plan for AIDS Relief (PEPFAR). ADVANCE is now at its halfway mark, and the meetings in Lusaka were designed to both take stock of the program’s accomplishments and to plan for its future success.

For decades, USAID has fostered leadership among African scientists. This long-term support, funneled through IAVI to its network of partner institutions, began in 2001. It helped establish a network of clinical research centers in five sub-Saharan African countries and India (see map, page 13). These clinical research centers are now actively engaged in basic science, epidemiological, and clinical research that is helping advance HIV vaccine design and development. USAID’s support also allowed IAVI to conduct large cohort studies of HIV-infected individuals in Africa that have provided some of the most useful clues for researchers who are working to design novel vaccine candidates (see page 18).

The ADVANCE program, the latest iteration of the now decades-long partnership between USAID and IAVI, places an even greater emphasis on shifting leadership to African investigators, or as Kamali describes it, allowing the program “to be

driven by Africans for Africa.” This involves further developing scientific research capacity on the continent by supporting young African scientists so they can become leaders in the global efforts to develop, test, and eventually implement a future HIV vaccine and other prevention strategies. Much of this work happens through ADVANCE’s Vaccine Immunology Science and Technology for Africa (VISTA) consortium.

The motivation for involving African scientists and populations in this work couldn’t be more obvious—Eastern and Southern Africa are still home to the largest number of people living with HIV, according to statistics from the Joint United Nations Programme on HIV/AIDS. There is arguably nowhere on earth that could benefit more from a long-lasting, highly effective vaccine.

ADVANCE is one of many ongoing efforts to cultivate promising African scientists. The Human Heredity and Health in Africa Consortium (H3Africa) is another example. This program aims to facilitate African scientists to conduct research into diseases on the African continent and to support a sustainable African research enterprise. There is a broad base of international support these days for public health and genomics research in Africa stemming from the support of various governments and organizations. There are also many terms used to describe the efforts to develop the scientific capacity of African researchers and institutions. The most common is probably capacity building. But, perhaps unsurprisingly, African researchers bristle slightly at this term.

“It’s almost, in a way, a depressing term,” says Moore. “It ignores everything that we have on the continent and all the successes we’ve had in the past. It is very well intentioned, but sometimes it’s slightly denigrating too,” though Moore acknowledges that South Africa is in some ways unique among sub-Saharan African nations. “South Africa is a little bit different because I think we have kind of a higher starting position in some respects.”



Capacity building has the connotation that you are building something from scratch, but actually, you are developing the capacity that is already here. So it’s not capacity building, it’s capacity development,

“



If you want scientists to stay in Africa and build their careers here, then they have to see a path, and that pathway is sometimes very, very hard to see when you’re a young scientist.

”

Kamali, a native of Uganda who oversees IAVI’s programs in Africa from its offices in Nairobi, Kenya, agrees that the term “capacity building” undervalues the significant intellectual resources and infrastructure that already exist across the region. “Capacity building has the connotation that you are building something from scratch, but actually, you are developing the capacity that is already here. So it’s not capacity building, it’s capacity development,” he says. “Whoever comes to Africa is finding the platform is already here, and they are just enhancing the capacity of individuals, institutions, and networks toward improving their capabilities to respond to their health needs.”

After decades of investment in developing the infrastructure, institutions, and human capacity to conduct scientific research in Africa, I asked Kamali and Moore how they measure the success of these efforts. “That’s a little complicated,” says Kamali. “There are traditional ways—number of people trained, number of Ph.D. candidates supported, number of post-docs trained—but they have their limitations.

“There are several more objective ways to measure success, including the number of African

scientists who assume leadership roles,” says Kamali. “The idea is that these individuals should be prepared to take over for the current generation that is leading research programs and institutions. We’ve trained these individuals and post-docs. The next measure of success is whether they will now be able to recruit and train another cohort of scientists themselves so that it is an effect that continues to build.

“Another measure of success is, of course, number of publications by African scientists in peer-reviewed journals, especially as first authors. I think that’s a very tangible measure.” Moore nods in agreement.

“Another is the number of grants that young African scientists apply for and receive as the lead grant holders. The other, which we keep talking about, is studies being led by African investigators.”

Earlier that day during the ADVANCE meetings, Eunice Nduati, a post-doc who studies B- and T-cell immune responses to early HIV infection at the Kenya Medical Research Institute Wellcome Trust Research Programme in the coastal town of Kilifi, Kenya, was asked how she defined

“
Rather than saying this product was tested to be safe in France and in Belgium and now it’s time to go to Africa, which has always caused problems for us, these are products that we have participated in developing right from the beginning.”

success as an African scientist. Her answer was simple: “Success for a scientist in Africa looks the same as it does for a scientist anywhere. It’s the same things that define success.”

Moore wholeheartedly agrees. “I thought that was a brave and accurate response. They are the same measures of success,” she says. “We need to have African-led research grants that are sourced by Africans from international grant-funding bodies, and those really are the same measures of success that any young scientists in the U.S. would also aspire to,” Moore adds.

“I also agree with the point Anatoli is making that we want these students to turn into the next set of leaders and to develop their own research programs.”

Nduati currently holds a mid-career fellowship from IDeAL (the Initiative to Develop African Research Leaders), one of 11 of the Developing Excellence in Leadership, Training, and Science (DELTA) Africa initiatives that are funded by the Wellcome Trust and the U.K. Department for International Development. She also is a part of the IAVI VISTA consortium, which is funded by USAID. Additionally, she has a grant from the sub-Saharan African Network for TB/HIV Research Excellence (SANTHE).

If you can wade through all those acronyms, you quickly realize that Nduati is one of the success stories. And she isn’t the only one (see pages 10-16). There are several others like her, a sign that the focus on developing the capabilities of African scientists and institutions is paying off. “If you want scientists to stay in Africa and build their careers here, then they have to see a path, and that pathway is sometimes very, very hard to see when you’re a young scientist,” says Moore. “Unless you have very generous mentors, it is sometimes hard to see how you can stay in Africa and do science. But now there are a lot of people finding that pathway. This has been happening for a long time, but I think it is certainly happening more now.”

Kamali acknowledges that there is still plenty of work to do to shift the balance to Africa, but the scientific progress on display from the young and mid-level HIV researchers suggests things are moving in the right direction. “We are not com-

pletely there yet, but I think that if we continue on the same track and at the same pace, we will get there.”

Part of what makes it easier for these young scientists to forge their careers in Africa today is the significant institutional capacity that has been strengthened over recent decades. The institutions, or, as they are sometimes referred to, centers of excellence on the continent, can now provide the support systems to conduct scientific research at the highest levels.

In a way, an individual’s success is dependent on the institution’s success. “I suppose institutional success is creating a system so that a young scientist can look at the institution and know that they can shape their career there and be safe in knowing that when they need to buy reagents, the systems are in place, and when they need to apply for grants, they have grant managers to help with that. It is also knowing that grant-funding bodies like the Wellcome Trust are going to know that their facilities are good enough to manage the grants once they are awarded,” says Moore. “Those should be the least of your worries as a young scientist. Your worries should be coming up with the cool ideas and innovative science. Institutional success is what allows a scientist to focus on science.”

The improved institutional capacity not only helps retain young African researchers on the continent, it also draws some of them back. “Once the institutional capacity has been developed, then you start seeing those institutions attracting African scientists from Europe and America back to Africa. It actually reverses brain drain,” says Kamali. “But that can only be achieved when African institutions meet a certain level and scientists can access everything they need to be able to do what they were to do if they were in the north.”

Another sign of institutional success is seen through South-to-South collaborations, which is when African institutions are partnering with each other or with institutions in India. “Much of the work is African institutions partnering with U.S. or European universities, which of course you can’t totally avoid,” says Kamali. “Nor do you want to avoid it,” Moore interjects.

Kamali agrees. “But you also want to see these research consortia develop between African institutions that are sharing expertise.”

There is a reigning sentiment of optimism in the HIV vaccine field today (see “Overflowing with Antibodies and Optimism,” *IAVI Report*, Vol. 22, Issue 3, 2018). Much of this optimism is driven by the work on broadly neutralizing antibodies—those relatively rare proteins that are capable of inactivating many of the currently circulating isolates of HIV.

These antibodies allowed scientists to identify new targets on the virus that they can exploit in vaccine design, and have opened up the possibility of using broadly neutralizing antibodies directly for prevention, a strategy referred to as passive administration or antibody-mediated prophylaxis. “All of the people who’ve worked on all of these things for so long have always hoped that at some point we will be at the stage where the science drives the questions enough to be able to start testing things that we think might actually work,” says Moore. “It is the type of blue-sky science that has finally translated into something that I think will be useful. I don’t think we’re expecting a panacea, but both the active and the passive immunization arms are hugely exciting and promising. Time will tell.”

Based on work that originated with HIV-infected African volunteers, some of these vaccine approaches and passively administered antibodies are, or will soon be, returning to Africa to be tested in clinical trials (see page 8). The significance of this is not lost on any African investigator. “I think many other people have the same sense of satisfaction from seeing these approaches come back to be tested in Africa. For me, it is the culmination of many years of work.”

It turns out that this HIV vaccine and antibody work also has more than its roots in Africa. “A lot of the samples were collected here, that’s true, but beyond that, a lot of the great science was done in Africa, including defining how these antibodies develop and defining how common they are,” says Moore. “It’s much more than just the fact that we have these incredible cohorts that people have built up over many, many years.”



Now researchers on the continent are contributing in yet another way toward the quest to develop an HIV vaccine. “Many African scientists are also involved in understanding whether these trials are going to work, which I think is exactly the model that we want to see,” Moore says. “These antibodies and vaccines will be tested here and people in African countries will be measuring the immune responses and seeing whether these concepts will work. That’s exciting.”

The fact that this work involves African researchers from the start may also positively affect eventual acceptance of any future products that are developed, according to Kamali. “Rather than saying this product was tested to be safe in France and in Belgium and now it’s time to go to Africa, which has always caused problems for us, these are products that we have participated in developing right from the beginning,” he says. “These products, modified or otherwise, are coming back to the populations from the countries where they were first isolated. If we are eventually successful, I think it would be a unique and historical discovery to show that this work started with the communities in need and then these products came back, are tested, and eventually delivered to these same communities.”

Historical indeed. ■

Penny Moore, a Reader and South African research chair of virus-host dynamics at the University of the Witwatersrand and the National Institute for Communicable Diseases, in the lab in Johannesburg.

The best is yet to come

Africa is contributing far more than samples to scientific research. The continent's scientists are actively engaged in developing and testing novel HIV vaccine candidates.

BY KRISTEN JILL KRESGE

In a few months, a novel HIV vaccine trial will begin enrolling volunteers in Kenya. This trial will test whether an engineered protein that mimics the shape and structure of HIV's outermost protein known as Envelope, or Env for short, can induce antibodies against the virus. As simple as that might sound, it took decades of work, and many failed attempts, to reach this point. And it all started with a Kenyan infant.

HIV is a notoriously difficult pathogen for many reasons. One is that the three-part or trimeric Env protein spikes that protrude from the virus' surface are rather unstable. Given the Env protein is the target of all antibodies against the virus, this was a major stumbling block for vaccine design.

Scientists struggled for many years to sufficiently stabilize the Env trimer. Many monomeric HIV proteins were tested in vaccine trials over the years instead, but none of them induced a broadly neutralizing antibody (bNAb) response against the virus. These highly specialized antibodies that can neutralize a broad swath of HIV isolates are what many researchers predict would be the best way to protect against the diverse strains of HIV currently circulating around the globe. Scientists suspected a better mimic of the native Env trimer would be a superior vaccine immunogen, but they were largely unsuccessful in their attempts to develop one.

It wasn't until six years ago that researchers successfully engineered a stable trimeric protein that accurately, though not exactly, mimics the native HIV Env spike (*PLoS Pathog.* 9(9): e1003618, 2013). This engineered trimer, dubbed BG505 SOSIP.664 gp140, was based on the HIV env gene from a clade A transmitted/founder virus—the viral variant that initiates an HIV infection—sample collected from a six-week old Kenyan infant who was involved in a mother-to-child HIV transmission study and who was infected with HIV at birth (*J. Virol.* 80, 835, 2006).

The BG505 SOSIP.664 gp140 protein was tested extensively in preclinical studies by a team of scientists directed by John Moore at the Weill Cornell Medical College, Rogier Sanders at the Amsterdam University Medical Center, and Andrew Ward and Ian Wilson at Scripps



The breakthrough buried in these letters

A structural model of the BG505 SOSIP.664 HIV Env protein superimposed on the amino acid sequence of the protein (see page 3). The ribbon diagram details the positions of the beta-pleated sheets, alpha-helices, and loops that make the BG505 SOSIP.664 HIV Env protein structure.

Structural model image originally published in *Viruses*, April 1: 10(4), 2018. Amino acid sequence originally published in *PLoS Pathog.* 9(9): e1003618, 2013.

“When we started, some people still thought you could not do Phase I vaccine clinical trials in Africa.”

Research (*PLoS Pathog.* 14(2): e1006913, 2018). Now, this BG505 SOSIP.664 gp140 vaccine candidate is being tested in the IAVI W001 Phase I clinical trial that already began in the U.S., and will soon begin enrolling volunteers in Kenya at the KAVI Institute of Clinical Research (KAVI-ICR) at the University of Nairobi.

And so the BG505 vaccine candidate, developed based on a virus isolated from a Kenyan infant, will return to Kenya. “Many of these products came out of African cohorts and are going back into African cohorts,” says Penny Moore, South African research chair of virus-host dynamics at the University of the Witwatersrand and the National Institute for Communicable Diseases, who studies bNAbS (see page 4). “This is what all of us, all of the people who have worked on all of these things for so long, have always hoped for,” she adds.

This vaccine candidate is one of the first native-like trimer immunogens to be tested in clinical trials, and the first to be tested in an African pop-

ulation. But the contributions of Africans won't stop there. Kenyan researchers will also be analyzing the antibody responses induced by the BG505 SOSIP.664 gp140 vaccine candidate, using many of the same highly sophisticated assays and tools that will be utilized by the U.S. institutions involved in the trial.

“This trial provides an opportunity to evaluate antibody responses to this vaccine in Africa, by African investigators,” says Devin Sok, director of antibody discovery and development at IAVI's Neutralizing Antibody Center (NAC) at Scripps Research in La Jolla, CA. Sok is working closely with researchers at KAVI-ICR to validate the assays and systems for this trial. “We want African scientists to be able to lead those efforts,” he says. “We are trying to shift the focus, the mindset, and the work to Africa.”

This wasn't always the case. Anatoli Kamali, head of IAVI's Africa program, recalls that in the late 1990s and early aughts, some people were skeptical about the viability of HIV programs in Africa.

Some experts in the field doubted it would be possible to provide comprehensive antiretroviral treatment programs or conduct high-quality HIV vaccine clinical trials in Africa. “When we started, some people still thought you could not do Phase I vaccine clinical trials in Africa,” he says.

Pontiano Kaleebu, director of the Uganda Virus Research Institute (UVRI) and the Medical Research Council/UVRI Uganda Research Unit, has been working with IAVI since 2001 to develop local capacity to conduct HIV vaccine trials and has witnessed dramatic progress. “It was our plan from the beginning that we needed to build capacity locally,” he says. Uganda was the first country in Africa to conduct an HIV vaccine trial in adults and also the first to conduct a pediatric HIV vaccine trial (*BMJ* 324, 226, 2002). “This was critical to showing that this could happen in Africa,” adds Kaleebu.

The clinical expertise that exists in Africa today has dispelled all doubts. “The exciting thing now

is African institutions and African scientists can do late-phase efficacy trials at the same standard as the north,” says Kamali.

But even after it became apparent that widespread treatment programs and gold-standard clinical trials were possible to implement and conduct in Africa, the role of African investigators was rather circumscribed. Clinical trials were often designed by researchers outside Africa, albeit with input from African principal investigators, and analysis of the trial samples and interpretation of the results was often handled by scientists in wealthier countries.

“Before, it was more about collecting samples in Africa and sending them elsewhere to be analyzed or researched,” says Vinodh Edward, chief operating officer for research at The Aurum Institute in South Africa. “Now what we are actually seeing is a number of young investigators being able to learn skills, either abroad or locally, and then being the ones who are actually doing the

Continued on page 13



RESEARCHER SPOTLIGHT

Eunice Nduati

To Eunice Nduati, success as a scientist isn't dependent on geography. The factors that define success—innovative research, a solid track record of publications, and the ability to attract ample funding—are the same for scientists everywhere, including Africa.

Nduati's interest in understanding immune responses to infectious diseases led her to study malaria at the Kenya Medical Research Institute (KEMRI) Wellcome Trust Research Programme in Nairobi. In 2005, she enrolled for her Ph.D. training in cellular immunology under the Biology and Pathology of the Malaria Parasite/EMBL International Ph.D. program, funded by the European Commission. This allowed her to spend time between the U.K. and the coastal town of Kilifi, Kenya.

After completing her Ph.D. studies, she returned to KEMRI in Kilifi to study B cells, a topic that continues to fascinate her. Nduati now has a mid-career fellowship from IDEAL (the Initiative to Develop African Research Leaders), a program based at KEMRI that aims

to develop outstanding African scientists into world-class research leaders. IDEAL is one of the 11 Developing Excellence in Leadership, Training and Science (DELTA) Africa initiatives that are a partnership between the Wellcome Trust, the U.K. Department for International Development, and the African Academy of Science's Alliance for Accelerating Excellence in Science in Africa.

Nduati is also a part of IAVI's Vaccine Immunology Science and Technology for Africa (VISTA) consortium, which is funded by the U.S. Agency for International Development (USAID). Her work involves studying HIV-specific B- and T-cell function in the early phases of infection and determining how this impacts the subsequent quality of the antibody response against HIV.

Nduati is focusing on fragment crystallizable (Fc) receptor-mediated antibody functions in particular, and is exploring whether these non-neutralizing antibody functions are associated with better viral control in infected individuals.

For this work, Nduati is using samples collected from cohorts of acutely HIV-infected African volunteers who were part of IAVI's Protocol C study (see page 20). As part of this project, she spent three months at the Ragon Institute of Massachusetts General Hospital, MIT and Harvard preparing to transfer cellular assays that are needed for this type of work to her home lab in Kilifi.

So far Nduati has found that very early on in HIV infection, Fc-mediated antibody responses are not significantly different in elite controllers—a small subset of HIV-infected individuals who can control viral replication without the use of antiretroviral drugs. Rather, it appears that individuals with progressive infection may develop better Fc-mediated immune responses over time.

Nduati is also engaged in preparatory work for the IAVI W001 trial that is testing the safety and immunogenicity of the native-like, trimeric HIV immunogen BG505 SOSIP.664 gp140. The trial is taking place at clinical centers in

Seattle and Boston, where enrollment has already begun, and at the KAVI Institute of Clinical Research (KAVI-ICR) at the University of Nairobi, where the trial is expected to start soon.

Nduati is part of the team that will be exploring immune responses to the vaccine candidate, including evaluating HIV-specific memory B cells in samples collected from vaccinated volunteers from Kenya and comparing them to those observed in volunteers from the U.S. clinical trial centers. The BG505 SOSIP.664 gp140 vaccine candidate is based on a virus originally isolated from a six-week old Kenyan infant (see page 8), and it will be the first engineered, trimeric HIV Env protein to be tested in Africa.

“This trial shows the strength of collaboration,” says Nduati. “It also offers an opportunity to tease out potential geographical-related immune differences, if any, that are important to consider for future immunogen design.” ■

“This trial shows the strength of collaboration. It also offers an opportunity to tease out potential geographical-related immune differences, if any.”



**RESEARCHER
SPOTLIGHT**

Eugene Ruzagira

In the early days of the HIV/AIDS epidemic, there was often not much a doctor could do but treat the hallmark infections that accompanied the development of AIDS. This was a time Eugene Ruzagira, assistant professor at the London School of Hygiene and Tropical Medicine (LSHTM) based at the Medical Research Council/Uganda Virus Research Institute (MRC/UVRI) and LSHTM Uganda Research Unit, recalls all too well.

“As a young medical student in Uganda in the late ’90s, there wasn’t much I could do for patients,” he says. “I just had to watch them waste and die.” This experience had a profound effect on the would-be malaria researcher, and soon he switched the focus of his research to HIV/AIDS.

In 2003, he joined MRC/UVRI, one of the African clinical research centers supported by IAVI through its cooperative agreement with the U.S. Agency for International Development (USAID), as a study coordinator. His work involved studying populations at high risk of HIV infection, including individuals in the remote fishing villages outside of Masaka, Uganda, along the shores of Lake Victoria. In these villages, HIV incidence is as high as 4-5%—up to four times higher than that of the general population.

It was at MRC/UVRI that Ruzagira met his long-time mentor Anatoli Kamali, former deputy director and head of the HIV Epidemiology and Prevention Research Program at MRC/UVRI, who now heads IAVI’s regional programs in Africa. “Eugene and I developed a successful mentoring partnership early on as a result of his excellent listening skills, intelligence, and articulate nature,” says Kamali.

Ruzagira eventually left his native Uganda to pursue his Ph.D. studies at LSHTM. In 2017 he completed his Ph.D. in epidemiology after just three years. He was awarded LSHTM’s Cicely Williams Prize for research advancing the health of vulnerable populations for his study on the importance of follow-up counseling in linking newly diagnosed adults to HIV care in

sub-Saharan Africa (*J. Int. AIDS. Soc.* 20(2), 25014, 2017).

He then returned to Uganda, intent on pursuing his career there, and rejoined MRC/UVRI. Now Ruzagira is overseeing preparations for a Phase IIb/III vaccine efficacy trial known as PrEPVacc, which will begin later this year in Uganda, Tanzania, Mozambique, and South Africa.

PrEPVacc is the first HIV vaccine trial to evaluate vaccine efficacy in the context of oral pre-exposure prophylaxis, or PrEP—the use of antiretrovirals to prevent HIV infection. This trial is a collaborative effort but one in which African investigators play a leading role, and Ruzagira feels fortunate to have the opportunity to be coordinating the trial.

“Being part of the PrEPVacc project has been a great opportunity for me to contribute to HIV vaccine evaluation in Africa, while interacting with and learning from world-class experts in the field,” he says.

The placebo-controlled PrEPVacc trial will test two combination vaccine regimens—a DNA candidate and HIV gp120 protein with an aluminum salt adjuvant, and a DNA/modified vaccinia Ankara (MVA) viral vector-based candidate with an HIV gp140 protein and a monophosphoryl lipid A (MPLA) adjuvant. The adaptive trial design will allow researchers to determine the safety and efficacy of the vaccine regimens in combination with PrEP, as well as the acceptability of daily PrEP use in these populations.

PrEPVacc will also evaluate two different PrEP drugs: Gilead Science’s Truvada, the only pill currently licensed for HIV prevention, and the company’s newer combination drug Descovy, which is currently only licensed for HIV treatment. Results from the large Phase III DISCOVER trial comparing the safety and efficacy of Descovy and Truvada for PrEP were reported recently at the annual Conference on Retroviruses and Opportunistic Infections (Abstract 104). These results indicate that Descovy is as effective as Truvada at preventing HIV infection and has a more favorable safety profile. ■

Continued from page 11

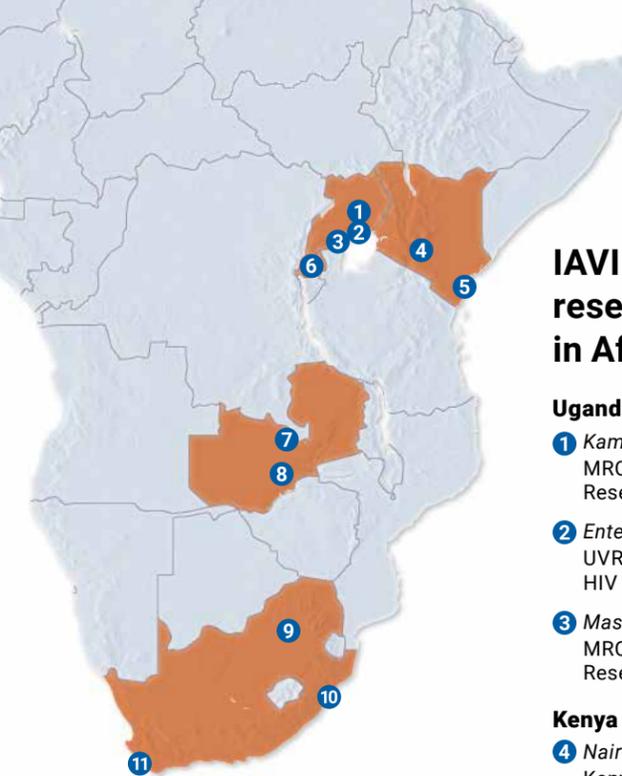
work on these samples. There has been a big shift and that is what excites me the most.”

This is precisely what will happen with the clinical evaluation of BG505 SOSIP.664 gp140. However, this is just one example of the increasingly important role African scientists and investigators are playing in HIV vaccine research today. Thanks to decades of investment in African institutions and investigators, there is now extensive infrastructure, a broad network of local and regional expertise, and a group of passionate and talented young researchers on the continent who are poised to contribute significantly to the goal of developing an HIV vaccine.

Eunice Nduati, a researcher at the Kenya Medical Research Institute (KEMRI) Wellcome Trust Research Programme in Kilifi, on Kenya’s coast, is one of the Kenyan researchers who will be analyzing memory B-cell responses and characterizing the neutralizing and non-neutralizing antibody responses induced by the BG505 SOSIP.664 gp140 vaccine candidate in the IAVI W001 trial (see page 10). “This is an exciting time for the HIV vaccine field,” she says.

Nduati is hopeful that conducting this trial in Kenya will allow researchers to identify any geographic differences in the immune responses generated by the vaccine candidate, which can then be taken into account for the design of future vaccine candidates. “We need to have a product that hopefully will be useful where it is most needed—on the African continent,” she says.

Many governments and international organizations support genetics and public health research in Africa today. But with regard to HIV vaccines, many researchers largely credit the nearly two decades-long partnership between IAVI the U.S. Agency for International Development (USAID) with developing the capacity of African clinical research centers and investigators. “There is no other partner that has been with Africa for 15 years,” says Eduard Sanders, a principal investigator at the KEMRI Wellcome Trust Research Programme, who is



IAVI clinical research partners in Africa

- Uganda**
 - 1 Kampala
MRC/UVRI and LSHTM Research Unit
 - 2 Entebbe
UVRI-IAVI HIV Vaccine Program
 - 3 Masaka
MRC/UVRI and LSHTM Research Unit
- Kenya**
 - 4 Nairobi
Kenya AIDS Vaccine Initiative—Institute for Clinical Research
 - 5 Kilifi/Mtwapa
Kenya Medical Research Institute; Centre for Geographic Medicine Research—Coast
- Rwanda**
 - 6 Kigali
Projet San Francisco
- Zambia**
 - 7 Ndola
Zambia Emory HIV Research Project
 - 8 Lusaka
Zambia Emory HIV Research Project
- South Africa**
 - 9 Rustenburg
Aurum Institute
 - 10 Durban
UKZN HIV Pathogenesis Program
 - 11 Cape Town
Desmond Tutu HIV Foundation

supported by IAVI through USAID. “That consistency is key.”

Beyond consistency, Edward sees something unique about the collaboration between IAVI and the network of clinical research center partners it helped create with USAID funding. “In my opinion, no one besides IAVI through USAID has been able to get the science taught and translated through African scientists. USAID and IAVI had faith in the people and the sites they were developing in Africa.”

This is perhaps best illustrated by IAVI’s ADVANCE (Accelerate the Development of Vaccines and New Technologies to Combat the AIDS Epidemic) program, which is funded by the current five-year cooperative agreement between IAVI and USAID through the United States President’s Emergency Plan for AIDS Relief (PEPFAR). The guiding philosophy behind ADVANCE, the latest installment of IAVI’s partnership with USAID, was to shift scientific research and leadership to Africa so that investigators there could drive the development of an HIV vaccine. “People in Africa needed to be taken seriously and given the opportunity to actually be able to do this work,” Edward says.

This includes providing young and mid-career researchers in Africa with the education, skills, and tools they need to conduct cutting-edge



RESEARCHER
SPOTLIGHT

Clive Michelo

For Clive Michelo, it was never a question of if he would return to Africa. “I always planned to come back to study malaria,” he says. But when Michelo was visiting his mother in his home town of Livingstone, Zambia, he heard about an open post-doc position at the Zambia Emory HIV Research Project (ZEHRP) in Lusaka. So instead of malaria, he returned to Zambia in 2015 from his Ph.D. studies in the Netherlands and began his post-doc work at ZEHRP.

Michelo’s project involves mapping HIV-specific CD8⁺ T-cell epitopes using transmitted founder virus sequences from acute infection samples collected from Zambian cohorts in Lusaka and Ndola. The goal of this work is to identify novel CD8⁺ T-cell epitopes in these early infection samples that are associated with viral control and could therefore be relevant to vaccine design within that population. Michelo also compares the local transmitted founder

virus sequences to the mosaic peptide antigens designed based on global HIV strains to determine if they differ.

To do this, Michelo sifts through hundreds of HIV Gag peptides designed from the transmitted founder viruses that were identified in IAVI’s Protocol C study (see page 20). He works with Andrew Fiore-Gartland at the Statistical Center for HIV/AIDS Research and Prevention (SCHARP) in Seattle on automating this process by using algorithms that can help predict potential T-cell epitopes. Michelo recalls that what took him three months of work, his colleagues at SCHARP could do in two hours. But he isn’t discouraged by this, saying he still has much to learn.

Even though he is the only post-doc at ZEHRP in Lusaka, which can be isolating at times, he stays connected to other post-docs

in IAVI’s Vaccine Immunology Science and Technology for Africa (VISTA) group, which, through funding from the U.S. Agency for International Development (USAID), supports Michelo’s post-doc work. He also interacts regularly with his collaborators at SCHARP and IAVI’s Human Immunology Laboratory, and his advisors Eric Hunter, a professor at the Emory Vaccine Center and in the department of pathology and laboratory medicine at the Emory University School of Medicine in Atlanta, and William Kilembe, project director and study physician at ZEHRP in Lusaka. Michelo is also part of the sub-Saharan African Network for TB/HIV Research Excellence (SANTHE) network, which also helps fund his post-doc research.

“It’s definitely been challenging. Sometimes you can feel like an island, but there is a definite research path, and the resources are

here. It is helpful knowing that IAVI and SANTHE are there to help you develop whatever you might be lacking,” says Michelo.

What inspires him most is that he is working on locally relevant research questions. His desk at the ZEHRP clinical research center in Lusaka sits in the same room where vaccine trial volunteers have their blood drawn. “It is really important knowing that I’m working on samples that are collected from the people we are seeing.”

So far, Michelo has found that the potential T-cell epitopes identified from 30 acute infection samples from Zambian volunteers matched up pretty well with those derived from global HIV sequences. But there was some variability. “That difference is something we can capitalize on to facilitate effective vaccine development for the local population,” he says. ■

“ Sometimes you can feel like an island, but there is a definite research path, and the resources are here. ”

“ We are trying to focus on things that haven’t been studied previously in the African context and that will contribute to the global efforts to develop an HIV vaccine. ”

science on the continent. This is the goal of IAVI’s Vaccine Immunology Science and Technology for Africa (VISTA) consortium within ADVANCE, a team of international researchers including Nduati.

Today, thanks to ADVANCE, the previous cooperative agreements between IAVI and USAID, and many other efforts to develop the scientific capacity of African researchers—including those by the Wellcome Trust, the U.K. Department for International Development, the sub-Saharan African Network for TB/HIV Research Excellence (SANTHE), the U.S. National Institutes of Health (NIH), the African Academy of Sciences, and many other governments and international funders—many say it is becoming easier for scientists to establish their careers in Africa (www.nature.com/articles/d41586-018-06971-4).

“There’s just a lot more support these days for doing that,” says Tom Hope, professor of cell and molecular biology at the Feinberg School of Medicine and professor of biomedical engineering at the McCormick School of Engineering at Northwestern University, who collaborates with inves-

tigators at the University of Nairobi on mucosal immunology research.

These early career scientists are able to link into a network of established African investigators, who are already making substantial contributions to understanding the pathogenesis, virology, and immunology of HIV, as well as efforts to develop vaccines and other prevention strategies. One of these mentors is Professor Thumbi Ndung’u, program director of SANTHE.

SANTHE, one of 11 of the DELTAS (Developing Excellence in Leadership, Training and Science) Africa initiatives funded by the Wellcome Trust and the U.K. Department for International Development, is actively engaged in developing scientific talent on the African continent. Ndung’u says years of funding from IAVI allowed SANTHE to establish its research on acute HIV infection, which then helped the group secure additional funding from the Wellcome Trust, the Bill & Melinda Gates Foundation, as well as the U.S. biopharmaceutical company Gilead Sciences, which is collaborating with SANTHE on HIV cure research. With this broad base of finan-

cial support, SANTHE is training 80 young African scientists in virology, immunology, and bioinformatics, including supporting many of the young investigators who are also receiving support through IAVI’s ADVANCE program.

“We have contributed a lot to HIV vaccine research as African investigators,” says Ndung’u. “A lot of the understanding of immune responses to acute infection was done by African scientists or in collaboration with African scientists.” Ndung’u also credits African researchers with helping to define the role CD8⁺ T cells play in disease progression, contributing to the identification of so-called elite controllers (HIV-infected individuals whose immune systems can control the virus without antiretroviral therapy), helping determine the role human leukocyte antigen plays in controlling HIV, and making contributions to describing HIV diversity on the African continent. “African scientists have also played a key role in identifying broadly neutralizing antibodies and in conducting vaccine studies,” he says.

Ndung’u and others, including Sok, are now preparing the next generation of African research-

ers to continue this work. For Sok, whose experience and knowledge belies the fact that he too is a young researcher, working closely with some of the early and mid-career investigators in Africa through IAVI’s VISTA consortium is rewarding. He particularly enjoys connecting young African researchers to the broader HIV research field and exposing them to others who can rigorously challenge their ideas. “That’s the way to become a better scientist,” he says. “Our goal is not to do me-too science in Africa and India. We are trying to focus on things that haven’t been studied previously in the African context and that will contribute to the global efforts to develop an HIV vaccine.”

For VISTA, this includes conducting basic science research to help develop both bNAb and T-cell based vaccines. The group is hoping to develop and advance a conserved HIV T-cell vaccine candidate into clinical trials within the next few years. Other VISTA projects include determining how the circulating viruses in different regions have changed over time, what impact viral recombination might have on vaccine design, whether there are geographic differences



RESEARCHER
SPOTLIGHT

Sheila Balinda

For Sheila Balinda, her mother was, and still is, her greatest supporter. In fact, it was her mother's suggestion that she might become a doctor that she thinks led her to pursue a career in science.

Balinda joined the Medical Research Council/Uganda Virus Research Institute (MRC/UVRI) in 2015 after receiving her Ph.D. in virology through a joint program between Makerere University in Uganda and the University of Copenhagen, which was funded by the Danish government's development cooperation Danida. Now she is in the midst of her post-doc at the MRC/UVRI and London School of Hygiene and Tropical Medicine Uganda Research Unit in Entebbe.

One focus of her research is characterizing the degree of viral recombination that is happening among newly HIV-infected individuals in the country. The virus in Uganda is primarily clades A and D, with some viral recombinants. But Balinda's research has shown that the majority (71%) of transmitted founder viruses—the viral variants that are responsible for establishing an infection—inferred from 30 acute infection samples collected from IAVI's Protocol C study were actually clade A/D recombinants. This striking level of viral recombination has obvious implications for vaccine design.

Balinda is now comparing these six- to eight-year-old samples from Protocol C with samples collected more recently to see how the viral dynamics may have changed in that time. Although the analysis is still underway, so far she is finding that there is still a high level of

in immune responses to vaccine candidates, and identifying more new bNABs.

Hope's team just received highly competitive grant funding from the NIH to pursue more mucosal immunology research with partners at KAVI-ICR and the University of Nairobi in Kenya, which they expect will help answer questions about some of the factors that enhance HIV transmission and dissemination (see page 22).

ongoing viral recombination, with both clade A/C and A/D recombinants identified from these more contemporary acute-infection samples.

To do this work, Balinda spent time at Emory University in Atlanta learning how to isolate and amplify whole viral genomes. She feels fortunate to work at MRC/UVRI and to have access to state-of-the-art equipment and facilities available at this virology center of excellence, including next-generation genetic sequencing, as well as generous and talented mentors both in Uganda and abroad.

But that doesn't mean there aren't any challenges. "The main challenge is getting the assays up and running," she says. During her time at Emory she felt she could solve any problem right away. "When you come back to Uganda, it's a completely different story. But it's through such experiences that you grow as a person and as a scientist."

Balinda is one of the post-docs in IAVI's Vaccine Immunology Science and Technology for Africa (VISTA) program, funded by the U.S. Agency for International Development (USAID) and is also the recipient of a path-to-independence award from sub-Saharan African Network for TB/HIV Research Excellence (SANTHE) that allows her to recruit and mentor a master's student. With this support, she is now forging her career as a virologist. "I'm hoping to become a principal investigator or group leader in a research area relevant to Africa, secure independent funding, and continue to grow." ■

Much of this work requires transferring technologies that were developed abroad to laboratories in Africa. Given some of the basic challenges of doing research in Africa, such as long delays in procuring reagents, this requires substantial time and resources. Scientists also have to deal with the complexity of standardizing assays across continents so the results, including those from the Phase I trial of the BG505 SOSIP.664 gp140 trimer and from future studies of even more com-

plex vaccine candidates and immunization regimens, are comparable.

But Sok and others say this investment is well worth the effort. "They already have so much knowledge and can contribute so much, we are just providing the resources to do it locally." And for many researchers, these cross-continent collaborations are mutually beneficial. Elise Landais, senior research scientist with IAVI's NAC, recalls traveling to Africa and being inspired by the group of young and motivated researchers she met there. "We have so much to learn from them," she says.

Hope also warns against assuming that partnerships with African researchers are a one-way street. "The mistake is thinking that science there is done at a different standard," he says. "When I started at KAVI, their flow cytometry was stronger than in my lab."

Robin Shattock, head of mucosal infection and immunity within the department of medicine at Imperial College London and the chair of ADVANCE's scientific advisory group, thinks the entire process of vaccine development should be a partnership. "Any vaccine should become something that is jointly developed," he says. "It should not be something that's coming from the northern hemisphere and then being applied in an African setting."

And on this point he gives ADVANCE high marks. "I think it's about getting the right mix of training, opportunity, buy-in, and aspirations to make everybody feel that they are a valued part of the process, and I would say that ADVANCE is ahead of the game with that and is a good blueprint for others to follow," he says. "For many other organizations, their default is still not to fully engage the potential of African partners. ADVANCE is a flagship approach for changing that dynamic, and what the program is trying to achieve is very laudable and clearly important."

Although many say there is still room for improvement. "You are now seeing more publications come from Africa and more African investigators get funded directly," says Ndung'u. "Yet, I don't think we are there completely. Compared to our colleagues in developed countries, there

are still fewer opportunities here," he says. "But we are beginning to see a shift."

This shift comes at a pivotal moment in the quest to develop an HIV vaccine. After decades of mostly disappointing results, researchers in the HIV vaccine field are increasingly, and somewhat uncharacteristically, optimistic. There are two ongoing vaccine efficacy trials, as well as an efficacy trial known as the antibody-mediated prevention, or AMP, study to determine whether direct administration of some of the recently isolated bNABs are effective at preventing HIV infection. All of these trials are taking place in Africa.

"The fact that we have these massive efficacy trials underway, more than we've ever had simultaneously, is hugely exciting," says Penny Moore.

There is also a new generation of vaccine candidates designed to kickstart the induction of bNABs, including BG505 SOSIP.664 gp140, which are or will soon be in clinical trials. "We are in this era of experimental medicine in which we are starting to ask questions about our immune system and how it actually responds to all of these engineered tools that we've come up with that are based on incredibly elegant experiments in the lab," she adds.

This is a much rosier picture than was the case 15 years ago. One of the major developments that brought the field to where it is today was the identification of new, more potent bNABs. This story also begins in Africa.

In 2009, scientists at IAVI's NAC reported on the isolation of two new bNABs, dubbed PG9 and PG16 that were identified from clade A HIV-infected volunteer in Africa (*Science* 326, 285, 2009; see figure, page 18). These antibodies were the first of now hundreds of new bNABs that have set off a new era in HIV vaccine development.

For decades, only a handful of known HIV-specific bNABs were available. To address this gap, researchers at IAVI, in collaboration with their partner network of clinical research centers (see map, page 13), set out to identify others. They did this by designing a large epidemiology study known as Protocol G. In this study, researchers collected blood samples from chronically HIV-

“

Any vaccine should become something that is jointly developed. It should not be something that's coming from the northern hemisphere and then being applied in an African setting.

”

“ Neutralizing antibody research is moving along at a pace that we couldn't have predicted 10 years ago. ”

infected individuals (infected for at least three years) across several continents, and then screened their sera for broadly neutralizing activity against a panel of HIV isolates. Researchers then isolated B cells from the sera samples that could neutralize the widest variety of viral variants.

This landmark study, funded by USAID, involved 2,100 volunteers, including many in sub-Saharan Africa. It led to the isolation of the antibodies PG9 and PG16, which were identified from a single Protocol G volunteer. These antibodies exhibited a remarkable ability to neutralize a broad swath of viruses, greater than any of the bNAbs previously identified, and were also very potent.

The discovery of PG9 and PG16 also set off a cascade of other developments that helped accelerate vaccine design efforts (see figure, right). Isolation of these two new bNAbs were integral to identifying the BG505 HIV isolate (*J. Virol.* 87, 5372, 2013). Scientists from IAVI's Vaccine Design and Development Laboratory in Brooklyn, NY, led by Simon Hoffenberg, utilized a bioinformatics approach to select the BG505 virus from the Los Alamos National Laboratory's HIV database because of its similarities to the virus strain that infected the individual from which PG9 and PG16 were isolated. "These samples [from Protocol G] were critical to that," says Landais. The identification of the BG505 virus isolate then led to the development of the BG505 SOSIP.664 gp140 native-like, trimeric protein that is now being tested as a vaccine candidate in the IAVI W001 trial. Other native-like trimeric HIV proteins that are now in clinical trials were also developed based on the BG505 viral sequence.

The engineering of BG505 SOSIP.664 gp140 in turn led to the first cryoelectron microscopy image of a native-like HIV Env trimer bound to an antibody (*Science* 342(6165), 1484, 2013), as well as the first crystal structure of this stabilized trimeric protein by scientists at Scripps Research, who are also part of IAVI's NAC, in collaboration with Sanders and John Moore (*Science* 342(6165), 1477, 2013). These detailed structural pictures of a native-like HIV Env trimer provided a blueprint for some of the structure-based vaccine design efforts that are underway today (see "Overflowing with Antibodies and Optimism," *IAVI Report*, Vol. 22, No.3, 2018).

HIV vaccine science comes full circle

Antibodies from Africa lead to African trial

In 2001, with support from USAID, IAVI initiates a large **multi-continent epidemiology study called Protocol G** to identify new HIV-specific broadly neutralizing antibodies to inform vaccine design efforts.

In 2019, the Phase I IAVI W001 trial of the BG505 SOSIP.664 gp140 vaccine candidate begins. This trial will enroll volunteers in the U.S. and Kenya, making it **the first native-like trimer vaccine candidate to be tested in an African population**. This trial is funded by USAID and the Dutch government, with additional funding from the Fred Hutchinson Cancer Research Center, Seattle HIV Vaccine Trials Unit; the Ragon Institute of Massachusetts General Hospital, MIT and Harvard; and the Bill & Melinda Gates Foundation. The BG505 SOSIP.664 gp140 vaccine candidate is not expected to induce broadly neutralizing antibodies against HIV on its own, but is an important step in understanding the types of immune responses that are induced by native-like HIV proteins in human volunteers. Researchers from Kenya will analyze the immune responses induced by BG505 SOSIP.664 gp140 and identify geographical differences, if any, in the responses to the vaccine candidate.

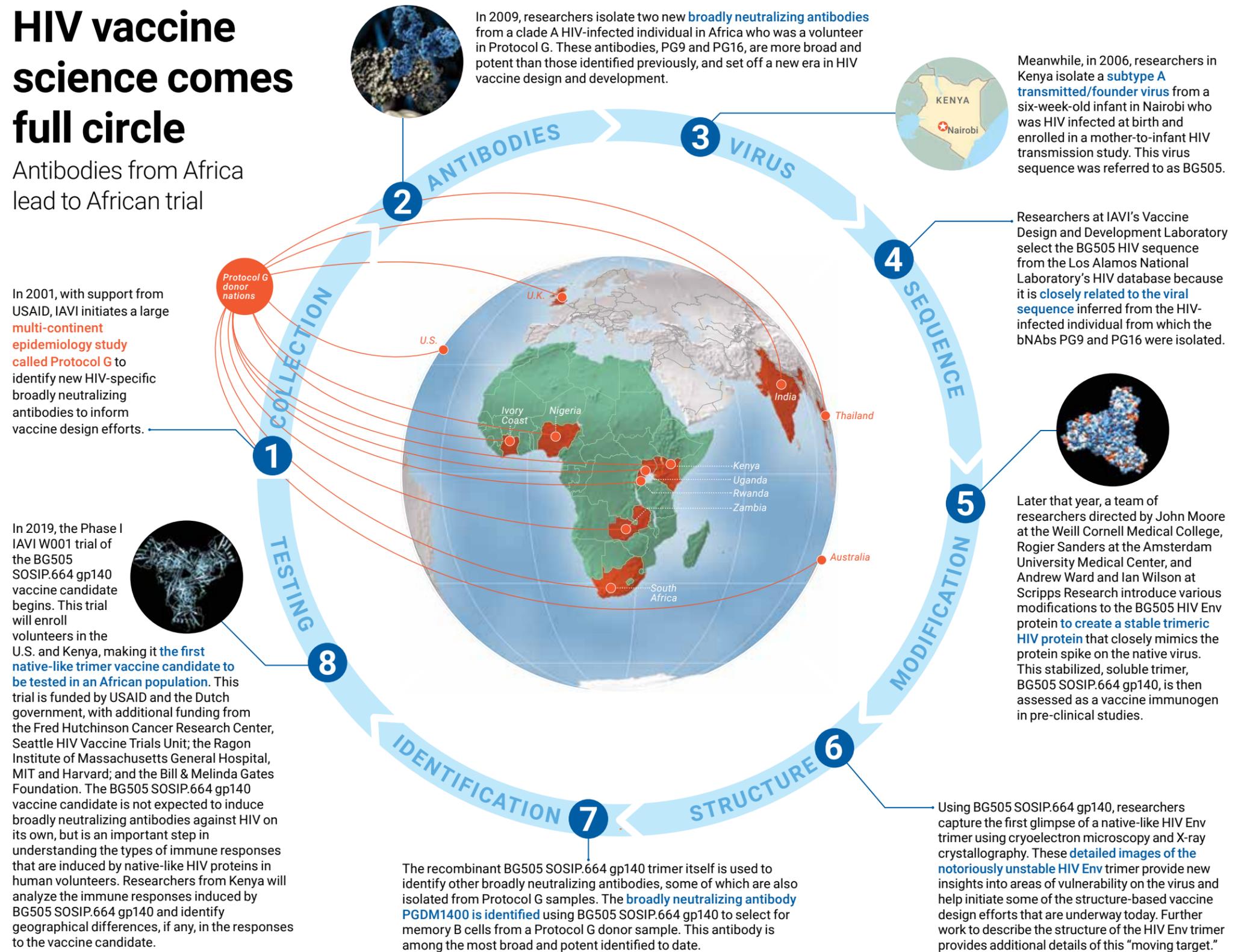
In 2009, researchers isolate two new **broadly neutralizing antibodies** from a clade A HIV-infected individual in Africa who was a volunteer in Protocol G. These antibodies, PG9 and PG16, are more broad and potent than those identified previously, and set off a new era in HIV vaccine design and development.

Meanwhile, in 2006, researchers in Kenya isolate a **subtype A transmitted/founder virus** from a six-week-old infant in Nairobi who was HIV infected at birth and enrolled in a mother-to-infant HIV transmission study. This virus sequence was referred to as BG505.

Researchers at IAVI's Vaccine Design and Development Laboratory select the BG505 HIV sequence from the Los Alamos National Laboratory's HIV database because it is **closely related to the viral sequence** inferred from the HIV-infected individual from which the bNAbs PG9 and PG16 were isolated.

Later that year, a team of researchers directed by John Moore at the Weill Cornell Medical College, Rogier Sanders at the Amsterdam University Medical Center, and Andrew Ward and Ian Wilson at Scripps Research introduce various modifications to the BG505 HIV Env protein to **create a stable trimeric HIV protein** that closely mimics the protein spike on the native virus. This stabilized, soluble trimer, BG505 SOSIP.664 gp140, is then assessed as a vaccine immunogen in pre-clinical studies.

Using BG505 SOSIP.664 gp140, researchers capture the first glimpse of a native-like HIV Env trimer using cryoelectron microscopy and X-ray crystallography. These **detailed images of the notoriously unstable HIV Env trimer** provide new insights into areas of vulnerability on the virus and help initiate some of the structure-based vaccine design efforts that are underway today. Further work to describe the structure of the HIV Env trimer provides additional details of this "moving target."



References: 2. *Science* 326, 285, 2009. 3. *J. Virol.* 80, 835, 2006. 4. *J. Virol.* 87, 5372, 2013. 5. *PLoS Pathog.* 9(9): e1003618, 2013; *PLoS Pathog.* 14(2): e1006913, 2018; *Viruses*, April 1: 10(4), 2018. 6. *Science* 342(6165), 1484, 2013; *Science* 342(6165), 1477, 2013; *Immunol. Rev.* 275(1), 21, 2017; *IAVI Report*, Vol. 22, Issue 3, 2018. 7. *J. Virol.* 90, 76, 2016; *Proc. Natl. Acad. Sci.* 111(49), 17624, 2014.



UVRI and IAVI staff on Kiimi Island, where they are recruiting women for the HPTN084 PrEP efficacy trial.

“Neutralizing antibody research is moving along at a pace that we couldn’t have predicted 10 years ago,” says Eric Hunter, a professor at the Emory Vaccine Center and in the department of pathology and laboratory medicine at the Emory University School of Medicine, who is also a member of ADVANCE’s scientific advisory group.

The stabilized BG505 SOSIP.664 native-like trimers also led to the identification of other bNAbs, of which there are now more than 200, including others isolated from Protocol G samples (*Proc. Natl. Acad. Sci.* 111(49), 17624, 2014; *J. Virol.* 90, 76, 2016). The PGDM1400 antibody, which is among the broadest and most potent identified to date, was isolated by Sok and colleagues from a Protocol G donor sample using the BG505 native-like trimer as bait.

Researchers have since amassed detailed information about how and where many of these antibodies bind to HIV Env, and in doing so have identified multiple targets on the virus that can be exploited by for vaccine design (*Retrovirology* 15, 61, 2018). It turns out that nearly the entire surface of the Env trimer is targeted by one or more bNAbs (*Immunol. Rev.* 275, 161, 2017). “Contrary to earlier perceptions, there are not just a few areas of vulnerability on the trimer, there are many,” write John Moore and Sanders. “The human immune system has found a range of different solutions to the problem of generating bNAbs.”

Now vaccine researchers are trying to come up with their own solutions to this problem.

Another pivotal epidemiology study was launched by IAVI in 2006, also with funding from USAID. The goal of this study, known as Protocol C, was to identify recently HIV-infected individuals and to follow them over time to determine markers of disease progression. The study enrolled more than 600 individuals from nine clinical research centers in Kenya, Rwanda, South Africa, Uganda, and Zambia for long-term follow up. From this cohort, researchers were able to identify acutely HIV-infected volunteers, sometimes within days of their contracting the virus, and determine how their immune systems responded to infection.

Researchers are still mining samples collected in Protocol C to explore many questions related to natural control of the virus and to garner clues about how to design a vaccine to induce protective immune responses. To date, more than 100 scientific publications have resulted from this single epidemiology study. IAVI’s DataSpace, a critical part of the ADVANCE program, is a bioinformatics project that collects all the clinical and immunological data and biological samples collected in Protocol C and makes them available to the broader scientific community (see www.iavi.org/our-work/clinical-epidemiology-research/hiv-epidemiology).

“We are sitting on this gold mine of samples that would be impossible to get today,” says Edward, who is also the principal investigator of IAVI’s Protocol C. “It’s highly costly following up a large cohort of people, and finding acute HIV infection is literally like finding a needle in a haystack. That’s what makes these samples so valuable.”

While the work to develop an HIV vaccine continues, investments in developing the scientific capacity in Africa are benefiting the broader field of public health research. “What HIV has brought is the understanding that research is important and that we must use what we have learned from HIV to address emerging infectious diseases and non-communicable diseases,” says Kaleebu.

The clinical capabilities to conduct HIV vaccine trials that were developed with IAVI’s support are now enabling UVRI to work in other areas of HIV prevention, including the Phase III HPTN 084 trial that is testing the long-acting antiretroviral cabotegravir for pre-exposure prophylaxis (the use of antiretrovirals to prevent HIV infection) in women at risk of HIV infection from the fishing communities surrounding Entebbe, Uganda (see photo, page 20). This clinical capacity is also allowing UVRI to extend its focus to other public health concerns, such as Rift Valley fever, according to Kaleebu.

This diversification is also on display at KAVI-ICR. Since becoming a clinical research institute in 2013, KAVI-ICR has been involved in clinical trials of Ebola vaccine candidates, as well as basic scientific research on newly emerging pathogens, antimicrobial resistance, and non-communicable diseases, such as cancer, with the goal of doing clinical trials of new anti-cancer molecules in the near future. “We are using what IAVI has helped us establish to work in more areas, with more diverse funding,” says Professor Omu Anzala, director of KAVI-ICR.

But even with a diversified research portfolio, one issue that concerns Anzala, Kaleebu, and almost every other African investigator you speak with is sustainability. “We rely on international funding,” Kaleebu says. “We are making efforts to increase funding from our local governments, and they have increased their funding, but not by enough.”

Now that extensive infrastructure has been built and more young scientists are being trained, the emphasis is on sustaining these advances, and identifying consistent research funding to support the careers of young scientists on the African continent. “Sustainability is a scary problem,” says Penny Moore. Kamali agrees. “Anything related to either disrupted funding or cessation of funding will have huge, huge implications.”

Penny Moore thinks the best way to ward against funding interruptions is to help young scientists become successful and confident enough to apply for and win large research grants that will sustain their work. This is part of the reason why efforts like ADVANCE, SANTHE, and Wellcome Trust

fellowships are vital. They support young researchers and help them reach the point that they can apply for and receive funding from large research grant-giving institutions like the NIH. This is what happened recently for Hope and Marianne Mureithi, chief research scientist at KAVI-ICR at the University of Nairobi, and their colleagues (see page 22).

This is USAID’s vision. “Some global funders who conduct research in Africa for product development see opportunity; at USAID we look at our African counterparts and see possibility,” says Margaret McCluskey, senior technical advisor for HIV vaccines at USAID. “These young, African pioneers are the future of HIV vaccinology, and we at USAID are very proud of them, and the small but important part USAID plays in facilitating their self-reliance and ultimate success.”

Mark Feinberg, president and CEO of IAVI, also sees African scientists playing a critical role in developing an HIV vaccine and recognizes the role IAVI and USAID play in helping to make this a reality. “The work being done in Africa is the starting point and the ending point,” he says. “The long-standing partnership between IAVI and USAID is enabling important scientific advances and helping build research expertise in Africa, particularly among young African scientists, who are essential for the long-term success of the AIDS response. PEPFAR, a program of unprecedented vision and impact, is facilitating this progress.”

When Edward reflects on the accomplishments of the young scientists who are part of ADVANCE (see Researcher Spotlights), he thinks the program is well on its way to achieving many of its goals. “If you had asked me if this would happen, I wouldn’t have believed it, but this shows what IAVI and ADVANCE have been able to achieve in just the last couple of years. If we continue this way, probably sometime between 2021 to 2026, you are going to see a lot of mind-blowing research coming out of Africa.”

Despite the many challenges, it appears that HIV vaccine research on the continent is thriving. “The goal is to bring the assets we have together to accelerate progress,” says Feinberg. “The best is yet to come.” ■

“If we continue this way, probably sometime between 2021 to 2026, you are going to see a lot of mind-blowing research coming out of Africa.”

Stopping HIV where it starts



Marianne Mureithi is part of a team of researchers that just received highly competitive funding to study mucosal immune responses to HIV in Kenya.

BY KARIE YOUNGDAHL

Marianne Mureithi wants to go back to the beginning. The goal, of course, is developing an HIV vaccine, but Mureithi, chief research scientist at the KAVI Institute of Clinical Research (KAVI-ICR) at the University of Nairobi, and her partners are convinced that to achieve this goal, they must first understand the earliest moments of HIV transmission.

For women in Africa, who represent more than half of new infections on that continent, this means studying, and visualizing, the mucosal tissues of the vagina and cervix and the immune responses that originate there, where the body's cells first come into contact with the virus following sexual transmission. This requires developing a deep scientific understanding of the mucosal environment of the female genital tract and the immune cells there that can be recruited or stimulated.

This is the focus of Mureithi's research since she returned to her home country of Kenya after completing her undergraduate and doctorate studies abroad. It wasn't a given that Mureithi would return to Kenya after completing her Ph.D. studies at the University of Bristol, U.K., and a joint post-doctoral research appointment at the Ragon Institute of Massachusetts General Hospital, MIT and Harvard, and the University of KwaZulu-Natal in South Africa. Like many young African scientists, she was unsure if she would find the right research project and sufficient funding there.

But in 2010, during her post-doc, she attended a scientific conference in the U.S. where she met the inimitable Professor Omu Anzala, who heads KAVI-ICR. "When he realized I was Kenyan, he said, 'You know, Marianne, you can come back to Kenya and do this science.'" When she was next in Nairobi over the Christmas holiday, she met Anzala again and this time toured KAVI-

ICR. He was persuasive, and the facilities and staff were impressive.

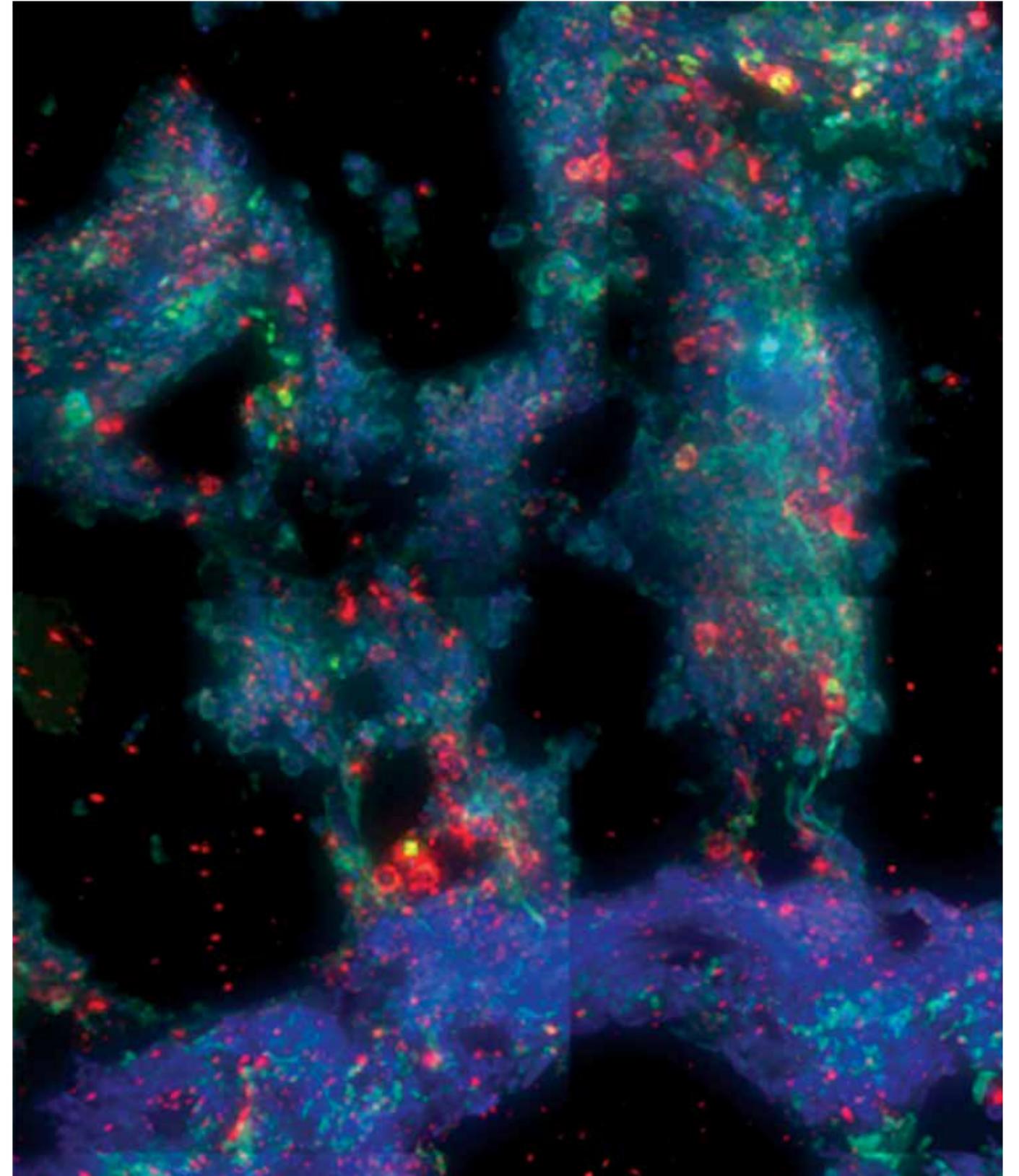
By the end of 2012, she was working in Nairobi. Further strengthening her ties to home, she met the man she would marry soon after her return. Now, eight years later, Mureithi has a busy and rewarding professional and personal life. She is a lecturer and research scientist in the Department of Medical Microbiology at the University of Nairobi School of Medicine, and is conducting research at KAVI-ICR with advanced tools and skilled collaborators across the world. She is also a mother of seven-year-old twins and a four year old.

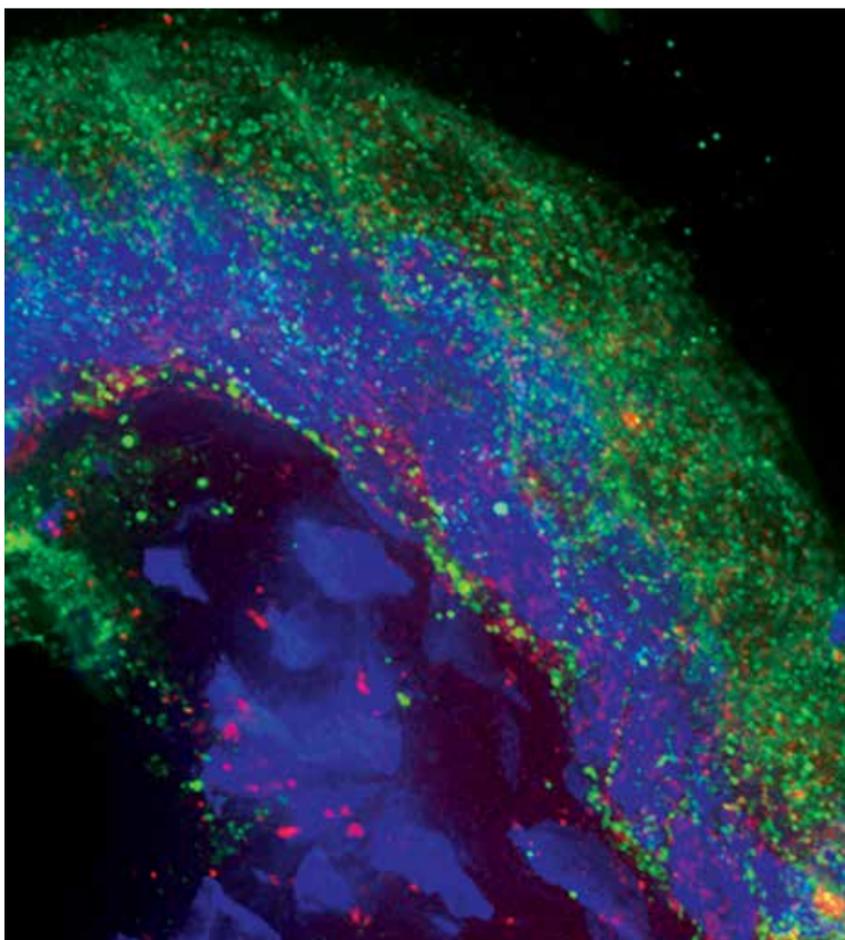
At the end of March, Mureithi and her international collaborators received funding from the U.S. National Institutes of Health (NIH) for a Research Project Grant, or R01, to study the crucial initial steps of HIV infection in the mucosal tissues that line the female reproductive tract, and to characterize factors that enable or inhibit HIV transmission and dissemination. This highly competitive grant funding will allow Mureithi and her colleagues to expand the scope of their ongoing work. Securing international research funding is also an important step in Mureithi's career.

The principal investigator of the project is Thomas Hope, professor of cell and molecular biology at the Feinberg School of Medicine and professor of biomedical engineering at the McCormick School of Engineering at Northwestern University. Hope is one of Mureithi's mentors. "The team there at KAVI is really good and their capability as a facility

Mucosal imaging

Immunofluorescence staining of a human rectal biopsy explant after infection with a clade C HIV. The staining reveals the localization of CD4 (red), CD3 (green), and cell nuclei (blue). Abundant CD3⁺, CD4⁺ helper T cells, the primary target of HIV, remain in the tissue after 14 days in culture with HIV. *Image provided by Robert Langat of KAVI.*





Immunofluorescence analysis of a cryosection of human endocervix. Localization of E-cadherin (green) reveals the columnar epithelium and cell nuclei (blue). Punctuate, spherical red signals are HIV particles containing photoactivatable green fluorescent protein, allowing virion detection in the tissue. Image provided by Akiso Matrona Mbendo of KAVI.

to understand where these signals are coming from and then what are the consequences—what are the changes they induce or reflect that lead to increased risk of infection?”

It is also becoming clear that many factors, including age, contraceptive use, diet, menstrual cycle events, and vaginal mucus may play a role in HIV transmission. “Our experience shows us that even mucus has a role, either to hasten transmission of the virus or to slow it down. We want to understand how it slows transmission down, and how we can influence the mucosal environment to slow it down even more to prevent infection,” says Mureithi.

There is also evidence that the microbiome likely plays a role. These are all elements Mureithi and the team plan to study further. As part of the pilot phase of the research, her team has collected samples from about 15 volunteers between the ages of 35 and 55. So far, emerging data suggests there may be some potential differences in the samples collected from Kenyan volunteers as compared to the samples Hope’s group obtains from U.S. volunteers. These differences could be due either to the virus, which in Kenya is predominantly clade C, or the host.

“What the consequences are of these differences we can’t say yet,” Hope says. “We’re just getting started here. All of these are important questions we need to probe.”

In one arm of the study, currently in pilot phase, the teams are collecting tissues from women who have had hysterectomies at Kenyatta National Hospital in Nairobi. A nurse from Mureithi’s research team waits outside the surgical theater to accept the tissue from the surgeon and transports the samples directly to the lab. Mureithi’s research scientists then introduce HIV into the tissue and observe the ensuing cellular events. Due to the fragile nature of the tissues, the team has about a 12-day window to work with each sample before it degrades.

Although experiments on HIV transmission and dissemination in non-human primates are informative, these human samples are critical. “The human experiments, ideally, have to be done in the places where it matters—where the HIV infection rates are highest and where the clades

and the tissues match up,” says Hope. “The only way for me to really accomplish that is to do exactly this: build capabilities and collaborations, first in South Africa and now in Kenya.”

Mureithi and her team capture images of how HIV infects and spreads through the tissue samples using a deconvolution microscope, one of few in Africa. The microscope, along with complex mathematical modeling software that Hope’s team has developed, allows the researchers to measure the kinetics of viral transmission and the distance viral particles travel from the initial site of infection. The Kenyan team has developed software to share videos of this process with the Northwestern team.

Mureithi and Hope both credit the team’s access to the deconvolution microscope with kickstarting the research that led to their R01 grant funding from the NIH. “The key moment was when we got approval from USAID [the U.S. Agency for International Development] for them to purchase a microscope to be housed there at the University of Nairobi. I’d been trying for years to get the microscopes we used into Africa, and in 2017 I finally got one moved from Bangkok that was originally supported by the Bill & Melinda Gates Foundation,” says Hope. “Then IAVI helped us to get the equipment set up in Nairobi, and the research took off from there. I think this R01 grant is an example of what can be leveraged from these investments by USAID and IAVI.”

Mureithi is also grateful to Margaret McCluskey, senior technical advisor on HIV vaccines at USAID, for introducing Mureithi to Hope’s team, which pioneered new uses of the deconvolution technology. “Her vision was for Tom and the KAVI team to grow together to look at the earliest events following HIV transmission,” says Mureithi. “Through this collaboration we’re learning a tremendous amount from each other—I’ve sent some of my young scientists to be trained at Tom’s lab, and he’s sent some of his scientists here.”

The access to equipment and other resources still varies; for example, Hope’s team has a positron emission tomography (PET) scanner they can use to study viral dynamics in multiple tissues simultaneously, a technology that is yet unavailable to Mureithi’s team. Still, she says, “The goal of USAID is that our teams will someday be on par,

and I think through these kinds of collaborations that can eventually happen.”

In addition to her research activities at KAVI, Mureithi teaches undergraduate, medical, and Ph.D. students. She uses her teaching platform to impress upon her students that the research happening in Kenya may eventually lead to an HIV vaccine. She even invites students to her monthly research meetings and is gratified that more and more students are attending.

Mureithi particularly enjoys working with Ph.D. students. She recalls that at the beginning of her appointment at the University of Nairobi, there were not many other Ph.D.-level scientists to supervise graduate students. “Now we have more scientists and more capacity to mentor.”

She hopes these efforts will help convince young scientists to stay in Africa and to pursue their careers where their expertise is much needed. Mureithi also welcomes scientists from other countries to pursue their research and teaching in Kenya. “These links and networks with other researchers will help our young scientists develop in their own research, be exposed to more funding opportunities, and have more opportunities to write grants,” she says.

If you look at her life from the outside, she acknowledges her days might appear quite hectic. “I am a full-time lecturer, I write exams, I conduct research, I write grants, and I go to conferences. And don’t forget, I’m also a mother: I have three children who are under 10 years old! It is a lot.” Yet Mureithi, who always has a ready smile, doesn’t dwell on her busy schedule. “I’m not a one-woman show. We have a fantastic team, and I have a fantastic mentor in Professor Anzala. I can cascade his mentorship to my team in the lab, and we all benefit. Occasionally it feels like all the balls are dropping, but that’s the exception, not the rule.”

In spite of the demands on her time and the challenges of keeping African scientists in Africa, Mureithi sees a bright future for herself and other researchers on the continent. “We have African problems that need African solutions. The more brains we have here working on the problems, the more progress we’re going to make on the HIV prevention front.” ■

“

We have African problems that need African solutions. The more brains we have here working on the problems, the more progress we’re going to make on the HIV prevention front.

”

Upcoming efficacy trial illustrates the value of African-led science

We must continue to engage local investigators and develop their capacity to conduct more basic and clinical research on the African continent.

BY KUNDAI CHINYENZE

In February, I visited Maputo, Mozambique, for the first time.

I went there to attend an investigators meeting for PrEPVacc, a Phase IIb/III efficacy trial that will start later this year in Uganda, Tanzania, Mozambique, and South Africa. This trial will test two regimens of experimental DNA, poxvirus, and Env protein HIV vaccine candidates administered in combination with oral pre-exposure prophylaxis (PrEP)—the use of antiretrovirals to prevent HIV infection.

PrEPVacc's design is novel. The trial aims to generate data on HIV vaccine efficacy, investigate correlates of protection, determine adherence to and acceptance of PrEP, and compare the efficacy of the experimental PrEP drug Descovy with Truvada, the only licensed PrEP drug.

This is the first trial designed to evaluate the efficacy of a vaccine candidate in the context of oral PrEP. PrEPVacc is also an African study. It is supported by European and American partners and funded by the European Union, but the trial database, trial management, and primary laboratory assays will be undertaken by African investigators.

Eugene Ruzagira, a senior scientist at the Medical Research Council/Uganda Virus Research Institute (MRC/UVRI) and London School of Hygiene and Tropical Medicine (LSHTM) Uganda Research Unit, is coordinating these efforts from Entebbe, Uganda (see page 12). It is by no means the first trial to engage African researchers—there is a rich scientific history here, certainly in the HIV vaccine field—but it will be the first efficacy trial that will be coordinated and centrally managed by an African organization across four countries. Instead of gathering samples to ship off for analysis somewhere else, local investigators, who understand the local context and needs of the

populations, will oversee this large and complicated HIV vaccine trial.

It has taken many years and much effort to get to this point. And it is just a hint of what is to come if we continue to engage with local investigators and develop their capacity to conduct more basic and clinical research on the African continent.

When the U.S. Agency for International Development (USAID) challenged us to launch a formal capacity-strengthening program at IAVI in 2014, it was both exciting and challenging. We set out to build the next generation of science leaders. We recruited early career researchers and aimed to develop independent, innovative investigators who are capable of addressing local and global public health issues, including contributing to HIV vaccine development and prevention research more broadly.

For the individual, this requires providing support to pursue advanced degrees, mentorship from senior scientists, and training in manuscript and grant writing so that they could fully develop the skills they need to succeed as independent researchers.

At the institutional level, it requires equipping local laboratories so that these investigators could conduct advanced science and clinical studies. This includes providing adequate funding, skilled labor, appropriate technology, as well as sufficient managerial and administrative capacity to plan, execute, monitor, and evaluate studies. Even in developed countries, amassing the resources required to undertake complex research endeavors is difficult. These difficulties are multiplied many times in sub-Saharan Africa.

Researchers starting their career paths here are now able to draw upon the extensive resources available at institutions such as the Kenya Medical Research Institute and KAVI Institute of Clin-

ical Research in Kenya, the MRC/UVRI and LSHTM Uganda Research Unit, Projet San Francisco in Rwanda, and the Zambia Emory HIV Research Program. Two decades of hard work to develop the laboratory, clinical, and bioinformatic capabilities of these institutions are now enabling scientists to function independently and make significant contributions.

Regional labs are now able to perform immunology assays, including T-cell epitope mapping, B-cell assays, flow cytometry, multiplexing, and viral immunome profiling. There are still plenty of constraints on the research infrastructure on the continent, but human resources have improved significantly and the technology is more advanced.

To date, IAVI's training programs have supported more than 42 advanced-degree candidates in HIV-related fields. Last year alone, 402 staff were trained in good clinical and good clinical laboratory practice. Scores of public health workers have received training and gained access to more advanced lab technologies. Hundreds of others are able to serve as frontline health care workers, having gone through regional trainings, including training in bioethics, mucosal sampling methods, long-acting reversible contraception services, and providing health services for key populations, such as men who have sex with men, female sex workers, and adolescent girls and young women.

Ten fellows have been accepted into IAVI's post-doctoral training program, focusing on immunology and virology research. These mid- or early career scientists are now contributing to the basic scientific understanding of the viruses and immune responses in African populations, and are contributing to efforts to design vaccine immunogens. These post-doctoral scientists have published their research and in many cases have gone on to secure additional funding, including path-to-independence grants from SANTHE—a sub-Saharan network of African-led research in HIV/AIDS and tuberculosis—and highly competitive fellowships and grants from the Wellcome Trust and the U.S. National Institutes of Health.

They are able to do this because of the financial support, training, and mentorship they have received. Gloria Omosa-Manyoni, a lecturer in the University of Nairobi's Department of Medical Microbiology, is one of these mentors. Omosa-Manyoni, who



Two decades of hard work to build up and fund the laboratory, clinical, and bioinformatic capabilities of these institutions are now enabling scientists to function independently and make significant contributions.

served as a principal investigator on an HIV vaccine trial, is one of several mentors in scientific writing, having trained at the University of California-San Francisco. She trains researchers on publishing their findings and how best to disseminate this information to other researchers and policymakers.

We recently held another course in scientific manuscript writing in Nairobi. Over time, this course and others like it will lead to more publications by African researchers. Of the number of peer-reviewed articles published with the help of IAVI's partnership with USAID, some 62% in 2018 had lead authors based in Africa or India.

The numbers are encouraging, but the success of all of these capacity-strengthening efforts is best illustrated by the people, including Omosa-Manyoni and Ruzagira. It takes years of focused resources to mentor, train, and equip a capable scientist. Through sustained efforts—from international and local partners alike—we are starting to see more and more contributions to HIV vaccine research come from this part of the world, from laboratories that are organized and managed by investigators who live and work here. It's been a long, sometimes difficult, and ultimately rewarding journey. One we must continue. ■

Kundai Chinyenze is senior medical director for IAVI based in Nairobi.



Upcoming HIV-related meetings

JULY 2019

STI & HIV 2019 World Congress

July 14-17 | Vancouver, Canada
stihiv2019vancouver.com

IAS 2019

July 21-24 | Mexico City, Mexico
www.ias2019.org

NOVEMBER 2019

17th European AIDS Conference

November 6-9 | Basel, Switzerland
eacs-conference2019.com

Vaccines R&D – 2019

November 18-20 | Boston, Massachusetts
unitedscientificgroup.com/conferences/vaccines

DECEMBER 2019

9th International Workshop on HIV Persistence during Therapy

December 10-13 | Miami, Florida
www.hiv-persistence.com

For a full list of meetings and their descriptions, go to www.iavireport.org/meetings.



Don't leave yet!

We want to know what you would like to see in future issues. Please share your thoughts by taking a brief survey on IAVI Report at <https://www.surveymonkey.com/r/WWL3JKY>