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GLOBAL HEALTH MATTERS

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Malaria network boosts U.S. government collaboration

By Judy Coan-Stevens

On June 18, 2024, researchers from across the U.S. government convened for the inaugural meeting of the Federal Malaria Research Network (FMRN). Cofounded by scientists from the National Institutes of Health (NIH) and the Food and Drug Administration (FDA), the network brings together representatives from various U.S.-led malaria efforts. The U.S. government is the single biggest investor in malaria control and prevention in the world. Getting a handle on all that is being done—from basic research in vector biology to malaria vaccine development and anti-vector implementation programs—is no small task. FMRN allows those working in programs across the entire U.S. government to see where investments are being made and how they intersect, leading to collaboration, knowledge-sharing, and amplification of each other's work.

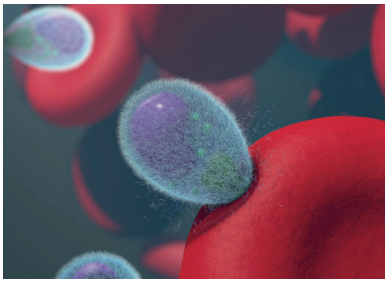


Image courtesy of NIAID

Malaria merozoites (green/purple) invading human red blood cells (red). Merozoites are covered in a fuzzy coating of surface proteins (light blue) that are shed during invasion.

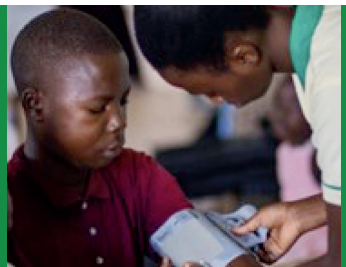
"We can be good spokespersons for the activities of our sister agencies that are doing amazing work," said Dr. Patrick Duffy, chief of the Laboratory of Malaria Immunology and Vaccinology at the National Institute of Allergy and Infectious Diseases, and one of the networks' cofounders. "We can also learn where there are gaps and successes, and how things fit together." A lot happens between the "upstream" basic research and the "downstream" implementation of malaria control and prevention. By sharing across the entire spectrum, researchers can make connections to their current and future work. If something is not relevant now, "it might be relevant to what's needed in the future for malaria control and prevention," added Duffy.

With a remit to enhance cross-governmental strategic collaborations and activities to advance global malaria control and elimination efforts, FMRN plans to convene regularly to share ideas, expertise, and findings pertinent to use-inspired malaria research (research meant for real-world application), from laboratory to field investigations and implementation and impact evaluation. Areas of discussion will focus on novel detection technologies and strategies, vaccines and other preventive and therapeutic interventions, including malaria parasite vector control, as well as new approaches to clinical trial design and monitoring of programmatic impact on malaria morbidity and mortality.

FMRN has been inspired in part by a previous entity called the Federal Malaria Vaccine Coordinating Committee. That committee was very focused on vaccine development, while FMRN has a wide interest in a range of issues, interventions and tools relevant to malaria control and prevention. "The genesis of this newer entity, rather than trying to coordinate activities, is to see more broadly across the whole U.S. government malaria effort," said Duffy, and to "make sure that we're not working at cross-purposes." One goal is that, with this network, researchers can speak knowledgeably about the malaria-based work that different U.S. government groups, such as USAID, The U.S. President's Malaria Initiative, CDC and NIH, are doing in a given country or region.

A broader goal is for those working within U.S. government agencies to gain more knowledge about the overall U.S. malaria footprint. "That knowledge can help us get the best return on investment with the research that we're doing," said Duffy. "It's really helpful for us to see how we can best direct our resources to near-term needs as well as to future long-term solutions."

FOCUS



Sickle cell research in Africa yields global benefits

Fogarty-supported research conducted by Dr. Siana Nkya in Tanzania, Dr. Adel Driss in Ghana, Dr. Sophie Kiguli in Uganda, and Dr. Halima Bello-Manga in Nigeria might help patients around the world.

Read more on pages 6 – 9

Neuzil engages with AFREhealth on global health

As a new director looking to develop her vision for Fogarty's programs around the world, Director Dr. Kathy Neuzil seized an opportunity to attend the seventh annual African Forum for Research and Education in Health (AFREhealth) Symposium in August to get feedback on barriers to obtaining funding, challenges and opportunities for research, and to establish rapport with its members. Supported by the National Institutes of Health (NIH) and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), AFREHealth is an interdisciplinary society that works with ministries of health, academic and training institutions, and other stakeholders to improve the quality of health care on the continent through research, education, and capacity building. It is African-focused and African-led.

As part of the Fogarty strategic planning process, Neuzil and Dr. UnJa Hayes, program officer for AFREhealth and other Fogarty programs, held a break-out session with AFREhealth investigators. Neuzil encouraged attendees "to share as many ideas as we can, openly and transparently."

Hayes explained how AFREhealth was shaped from the successes the Medical Education Partnership Initiative and the Nursing Education Partnership Initiative, earlier investments by NIH and PEPFAR to improve health care in Africa by strengthening its health and research workforce. Two years later, a Fogarty grant (in partnership with PEPFAR) funded the development of the necessary infrastructure to establish the society, which includes individuals, institutions, associations, and networks from all geographic and linguistic regions of Africa plus external members. "The listening session helps us see where there may be a disconnect—what is generally understood by the community as opposed to what we think we are communicating," said Hayes.

Research training

Education dominated the thoughts of many attendees. Fogarty currently features a variety of training programs, including bioethics, bioinformatics, infectious diseases, HIV, and trauma and injury research. One attendee noted that research training grants usually "focus on a single disease, but we need some funding that is broad spectrum—that allows people to study various

Fogarty Director Dr. Kathy Neuzil leads a listening session at AFREhealth's seventh annual symposium.

Photo courtesy of AFREhealth

conditions." Another attendee commented that caring for patients with noncommunicable diseases becomes an extended responsibility for most families. "In Uganda, someone who is caring for a patient with cancer often ends up with hypertension because of the stress," she said. "Can we think of a toolkit or policy brief or training of family members to help in that area?" Neuzil and Hayes encouraged innovative research projects that address these real-world challenges.

Fogarty currently features a variety of training programs in bioethics, bioinformatics, infectious diseases, HIV, and trauma and injury research.

Meanwhile, a family physician commented that she's most "concerned about strengthening the primary health care system because that's the first point of contact that we have and that's our engagement with the community—that's where we need grants. What about continuity of care, comprehensiveness, coordination, person-centeredness? Perhaps there are gaps there."

Grant management

The nuts and bolts of grant mechanisms also took center stage. A research administrator said she's benefitted "a lot" from NIH YouTube educational videos but sees a gap "in training us—the research managers and administrators—so that we can keep pace with dynamic research and any new requirements." (Fogarty currently offers funding for infrastructure development training programs for HIV research to help low-and middle-income country institutions build administrative capacity.) She also wondered if Fogarty might fund more studies of African traditional medicine.

In conclusion, Neuzil said, "This has really exceeded all expectations. So many people participated and gave us great ideas. I'm grateful to you all."

APTI's third cohort looks toward their second year

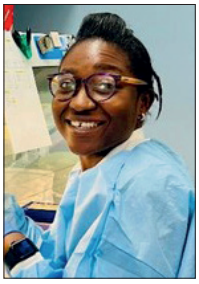
The African Postdoctoral Training Initiative (APTI) is a joint effort by the African Academy of Sciences, the Bill & Melinda Gates Foundation and the National Institutes of Health that aims to bolster Africa's scientific research capacity. Members of APTI's third cohort of fellows met in September to present their research. We caught up with four fellows as they reflected on their APTI journey.

DR. GILDAS HOUNMANOU

Dr. Gildas Hounmanou studies environmental microbiomes and disease outbreaks in Benin.

Dr. Gildas Hounmanou leads a study in Africa's largest lake village near Lake Nokoué in Benin exploring the connection between human microbiota and environmental microbiomes. His research focuses on how disease-causing microorganisms persist and spread between humans and the lake's ecosystem. By examining environmental exposures, seasonal changes, and human activities, the study aims to uncover factors contributing to outbreaks of diseases like cholera, typhoid, and water-related skin diseases, while also considering the impact of climate change on these waterborne epidemics.

Through the APTI program, Hounmanou has gained advanced skills in computational biology, including metagenomics and machine learning, crucial for his goal of establishing a research program on climate-sensitive infectious diseases in vulnerable communities.

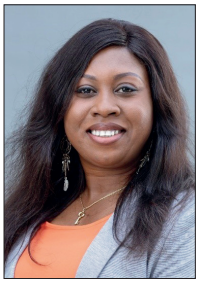


DR. VINIE KOUAMOU

Dr. Vinie Kouamou studies HIV drug resistance and mechanisms of HIV persistence in CD4+ T Cells in Cameroon

Dr. Vinie Kouamou credits her interest in HIV research to her late mother who was a laboratory scientist. As part of her APTI project with the National Institutes of Allergy and Infectious Diseases (NIAID), she is investigating how defective HIV-1 proviruses, a form of a virus that is integrated into the genetic material of a host cell but is unable to produce an intact virus, continue to trigger immune responses. This can lead to chronic inflammation among people living with HIV that are on antiretroviral therapy (ART), even though ART suppresses the immune system.

Through the APTI program, Kouamou has learned advanced scientific concepts and methodologies in virology, immunology, and vaccinology, skills vital for her preparation for pursuing independent research in the future. She plans to conduct independent research that contributes to health policies in Africa.



DR. CARINE KUNSEVI-KILOLA

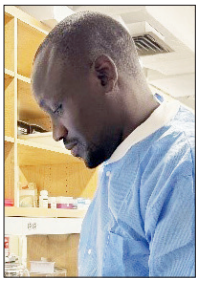
Dr. Carine Kunsevi-Kilola studies HIV and malaria in pregnancy in the Democratic Republic of the Congo

Before joining the APTI program, Dr. Carine Kunsevi-Kilola served as a postdoctoral research fellow at the Reproductive Immunology Research Consortium in Africa (RIRCA), based at Stellenbosch University, where her research focused on investigating the effects of HIV and antiretroviral therapy (ART) on pregnancy outcomes and child development.

Through the APTI program, Kunsevi-Kilola is expanding her research to explore the role of certain proteins on the surface of immune cells (called complement components) in shaping the immune responses to HIV and malaria infections during pregnancy, specifically in the plasma of malaria-infected women.

She says the APTI program has equipped her with valuable technical skills like proteomics and pathway analysis, which will help her reach her ultimate goal of continuing research in reproductive immunology or related fields, focusing on topics like HIV, malaria, and pregnancy outcomes.

DR. AMADOU NIANGALY



Dr. Amadou Niangaly conducts molecular surveillance of malaria in Mali

Dr. Amadou Niangaly started his biomedical research career in the early 2000s, when he received a PhD in parasitology-mycology and medical entomology from the University of Bamako, Mali. He's currently an associate professor at the University of Sciences, Techniques and Technologies, also in Bamako.

During the first phase of his APTI fellowship, he has been using genomic analysis to understand how the malaria parasite adapts to vaccines, drugs, and monoclonal antibodies. So far, Niangaly has learned critical skills in next-generation sequencing and molecular surveillance, which he plans to apply to infectious disease control in Africa and ultimately establish a genomics laboratory at his institution in Mali.

PROFILE

Monitoring HIV drug resistance in Zimbabwe

Justen Manasa, PhD

Fulbright Fellow:	2016-2017
U.S. institution:	Stanford University
Foreign institution:	University of Zimbabwe
Research topic:	HIV drug resistance
Current affiliation:	Senior lecturer and biomedical scientist, University of Zimbabwe

Dr. Justen Manasa says he had to "grow up quickly" over the last few years. As a senior lecturer and biomedical scientist at the University of Zimbabwe and director of the University's Innovation Hub, he watched as COVID-19 took hold in the region and ultimately took the lives of two of his closest mentors, the late Drs. James Hakim and David Katzenstein, both highly regarded in their fields. Manasa says, "These were people whom I admired and looked up to my entire career, and almost overnight, I was thrust into a leadership position to try and fill their shoes."

Manasa joined the Fogarty Global Health Fellows and Scholars program, now known as LAUNCH, through the Global Health Equity Scholars Program at the University of California Berkeley. Prior to his fellowship, Manasa had received support from Fogarty that allowed him to pursue his master's degree in molecular virology through a partnership between Stanford Medical School and the University of Zimbabwe. While at Stanford, Manasa participated in SPARK, a translational research program that bridges academia and industry by identifying research products from the academic community that have the potential to be taken to market as therapeutics, diagnostics, or medical devices. Essentially, the program helps the academics who created these products transition to entrepreneurship. While at Stanford, Manasa began to study HIV drug resistance which has been a research priority for him ever since.

In his Fogarty fellowship project, he focused on studying the increase in HIV drug resistance and providing equitable access to diagnostics to improve the effectiveness of treatment for patients. Monitoring HIV drug resistance is essential to determining how to improve treatment outcomes and which antiretroviral (ART) drugs are included in public health treatment regimens. Manasa's project aimed to leverage the advances in sequencing and bioinformatics technologies to provide increased understanding of HIV drug resistance among patients in Zimbabwe.

Following these experiences, Manasa learned that the University of Zimbabwe planned to transition their educational system to focus not only on teaching research and community service but also on innovation and industrialization. Like the SPARK program, the Innovation Hub at the University of Zimbabwe draws from academic research projects to develop products or services that have the potential to improve health. The hub then helps identify funding sources to transition the projects from academia to the market. Manasa knew this would be a natural fit for him.

Today, along with directing the Innovation Hub, Manasa serves as principal investigator for the Enhancing Non-communicable diseases (NCD) Research and Innovation Capacity or ENRICH program as well as a separate program focused on HIV genomics. With the long-term goal of generating evidence for interventions to improve care for people with NCDs in the region, ENRICH aims to train master's, PhDs, and postdoctoral candidates in Zimbabwe to be proficient NCD researchers.

Within his many roles, Manasa hopes to incorporate and implement what he learned from Drs. Hakim and Katzenstein. "One of the biggest lessons I learned working with them is that mentorship is key to the flourishing of trainees, and if you have good mentors as a trainee, you will flourish academically and in every other aspect of your life."

These days Manasa is based in Lesotho, South Africa, where he continues his pursuit of ensuring treatment for HIV remains equitable and accessible for patients throughout southern Africa as well as around the globe. In his free time, he is brushing up on his public health skills by pursuing a master's degree at the Harvard T. Chan School of Public Health. He is also working on a paper highlighting the impact that Fogarty programs have had on the research infrastructure in Zimbabwe.

Q&A

KAIYUAN SUN, PHD

Dr. Kaiyuan Sun earned a PhD in physics at Northeastern University. Dr. Sun's dissertation focused on complex system modeling of infectious disease dynamics. He joined Fogarty in 2018 as a postdoctoral visiting fellow and has worked as an in-house research scientist in the Division of International Epidemiology and Population Studies (DIEPS) since 2021. He has studied pathogens that cause global public health emergencies, including Ebola, Zika, and SARS-CoV-2, and is particularly interested in using mathematical models to translate findings of epidemiological studies into population-level impact and to inform public health decision making.

Why focus on infectious disease modeling?

If you think about infectious disease, it's kind of like a perfect system to reflect biological complexity. There's the human population (host) and a pathogen, and there's this arms race between the two, right? The pathogen will infect us and then it will evolve to evade immunity and to find as many ways to infect as many hosts as possible. From the human perspective, we can mount an adaptive immune response to a pathogen, and that either lessens the severity of response to the pathogen (disease) or prevents infection altogether. Humans also have the advantage of the invention of vaccination, so we can start the arms race even before pathogens infect us!

What are the findings from your recent *Nature Medicine* paper?

This study is unique because we're looking at immunity induced by prior infections—not immunity induced by vaccines—and how that might protect us in the future. We're also using a "correlate of protection," which is an immune biomarker that can reliably predict the extent of protective immunity. For example, seeing neutralizing antibodies in your blood indicates that you've already been exposed to an infection; and higher titers should mean better protection against a future infection.

We did this study when two SARS-CoV-2 variants—delta and omicron—were circulating in South Africa. So, we measured the neutralizing antibody titers prior to the delta wave and prior to the omicron wave and then we looked at how those titers potentially protected against reinfection. Our study confirms that neutralizing antibody titers correlate with protection against SARS-CoV-2, just as previous studies of vaccine-derived immunity showed.

The more interesting finding, however, is that the neutralizing antibody titer levels don't explain the majority of protection. For the delta wave, they explain just one third of the protection, while for the omicron wave, they explain even less: just 10%.

What does this mean?

This raises the question, What provides the remaining protection and what immune markers correlate with that? We need to look at other compartments of adaptive immunity and how they protect us against SARS-CoV-2 instead of focusing exclusively on neutralizing antibodies. For example, recent flu studies show immune markers like T cell response or innate response correlate with protection independent of neutralizing antibodies.

What's PHIRST? Why is it so special?

Our study of infection-induced immunity would not be possible without the groundbreaking design of PHIRST—the Prospective Household cohort study of Influenza, Respiratory Syncytial virus, and other respiratory pathogens community burden and Transmission dynamics in South Africa. The PHIRST studies are the genius of Dr. Cheryl Cohen's team at NICD (National Institute for Communicable Diseases), South Africa.

To understand the transmission of respiratory viruses, Cohen's team set up cohorts of people who get twice weekly PCR testing for influenza and RSV, irrespective of symptoms. In an early PHIRST study of influenza, Cohen's team found that asymptomatic influenza infection and transmission are much more common than we previously thought.

When the SARS-CoV-2 pandemic hit, they swiftly adapted their preestablished cohort infrastructure and protocol to create the PHIRST-C study (where "C" represents "COVID-19").

What's next for you?

A priority is to share my knowledge and expertise in mathematical modeling with my brilliant South Africa colleagues. I'm working closely with Dr. Jackie Kleynhans, a scientist on the PHIRST team, to model the impact of influenza vaccine and the potential impact of introducing pediatric vaccines to reduce influenza transmission.

Sickle cell research in Africa yields global benefits

Health care workers monitor the blood pressure of a person with sickle cell disease.

Photo courtesy of Badru Katumba/WHO

More than 100 million people worldwide are living with sickle cell trait. Between 2000 and 2021, the number of babies born with sickle cell disease (SCD) surged by 13.5%, with increasing rates reported in nearly every nation studied. According to the Global Burden of Disease Study 2021, the highest SCD disability burden was concentrated in western and central sub-Saharan Africa and India.

SCD is a genetic mutation that causes red blood cells, which are typically round, to form more like crescent moons. Round red blood cells move quickly through the blood vessels, but these sickle-shaped cells can impair blood flow and result in blood clots and poor oxygen levels, leading to chronic, acute pain syndromes, severe bacterial infections, and tissue death. Someone who is a carrier of sickle cell trait does not suffer from SCD; however, they will likely pass that gene on to their children, who may potentially suffer from SCD as a result.

Between 2000 and 2021, the number of babies born with sickle cell disease (SCD) surged by 13.5%, with increasing rates reported in nearly every nation studied.

Currently, there are several treatment options available for SCD. In 2023, the U.S. Food and Drug Administration approved two new gene therapies to treat SCD that can either add a modified gene to the body or make changes to a gene that is already in the body. The existing and new therapies reveal the scientific advances that have been made, yet they can be cost-prohibitive for many patients in high-income countries—and even more so in low- and middle-income countries.

Tanzanian research

Dr. Siana Nkya of Tanzania, a senior lecturer at Muhimbili University of Health and Allied Sciences (MUHAS) and president of the Tanzanian Human Genomics Organization (THGO), studies the genomic determinants of SCD in sub-Saharan African populations. Nkya, a former Fogarty Global Health Fellow, has spent the last 15 years of her career studying the effects of fetal hemoglobin decline among infants with sickle cell disease, a key factor in modifying the severity of sickle cell disease.

She recently completed a five-year project through an Emerging Global Leader Award funded by both NIH and Fogarty. This project involved establishing a birth cohort of more than 250 infants to study the natural decline of fetal hemoglobin in both sickle cell and non-sickle cell infants. The study tracked the hemoglobin levels of these infants from birth up to 3 years of age, providing critical insights into how fetal hemoglobin declines more slowly in infants with SCD compared to those without it. This delayed decline, or "delayed switch," is vital for understanding how to develop effective interventions, such as the timely administration of hydroxyurea.

Nkya's work has not only contributed to a better understanding of SCD but also laid the groundwork for future research and policy development in genetics across Africa.

Recently, the National Human Genome Research Institute (NHGRI) published a study highlighting that genetic carriers for sickle cell trait are prevalent across diverse human populations, including those of Mediterranean, Indian, and Middle Eastern ancestry, not just those of African origin. Other recent studies have also shown a marked increase in SCD prevalence birth rates in Latin America and the Caribbean. Fogarty-supported research in genomics and other disciplines conducted by Dr. Adel Driss in Ghana, Dr. Sophie Kiguli in Uganda, and Dr. Halima Bello-Manga in Nigeria also might contribute to the knowledge base that helps patients with SCD around the world.

Nkya said, "The more we support research in Africa, it's not just for Africa. It benefits the globe."

Probing the interaction of sickle cell disease and malaria resistance in Ghana

Sickle cell disease (SCD) is a genetic condition caused by a mutation in one of the genes that controls hemoglobin, the protein in red blood cells that transports oxygen. People with sickle cell trait—those who carry one mutated allele of the sickle cell gene—are protected against severe malaria. This unusual interaction between a genetic disease and a parasitical infection transmitted by mosquitoes intrigued Dr. Adel Driss during his 2014 Fogarty Global Health Fellowship.

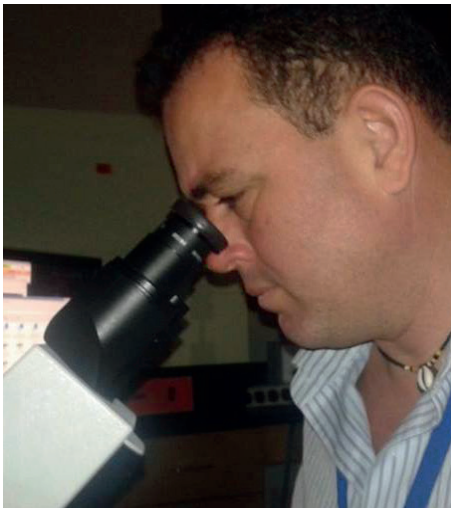
His fellowship at the Noguchi Memorial Institute for Biomedical Research in Ghana led to his Fogarty International Research Scientist Development Award (IRSDA) project, which investigated the molecular factors underlying the complex relationship between SCD and malaria resistance.

Molecular deep dive

Driss, an assistant professor at Morehouse School of Medicine, split his IRSDA project time between field research in Ghana and performing lab experiments and data analysis in the U.S. The relationships he established as a fellow helped him in his immersive investigation. Specifically, he investigated how microRNAs, small molecules in the blood that regulate gene expression, may play a role in protecting individuals with sickle cell trait from severe malaria. This study involved collecting blood samples from individuals with various sickle cell genotypes to examine whether microRNA levels fluctuate during malaria infection. ("Sickle cell genotype" refers to the specific abnormal hemoglobin gene a person inherits—there are a few different types.) Driss also conducted lab experiments and mouse model studies to explore how microRNAs affect malaria parasites in red blood cells. "For example, if we increase the expression level of a specific microRNA, will that enhance or inhibit malaria parasite growth?" he explained.

His project, scheduled to run from September 2016 to August 2021, was extended to March 2022 due to COVID-19 disruptions. The early years were productive, with almost 900 samples collected and progress made on the study's objectives. Later, pandemic restrictions prevented travel and fieldwork in Ghana and limited lab access in the U.S. Despite challenges, he and his colleagues achieved key milestones. Their findings included identifying differences in microRNA expression across various hemoglobin genotypes. They also showed that malaria parasites in red blood cells derived from donors grew at different rates (in petri dishes) depending on the donor's hemoglobin genotype.

"Additionally, we identified miR-451a, a microRNA, as a potential new player in the pathogenesis of malaria and SCD," said Driss. Though he's still preparing final results for publication, six articles have already been published in high impact journals. Overall, his findings enhance the understanding of the relationship between microRNAs, SCD, and malaria. Possible long-term outcomes of this work include development of new therapies, interventions, and diagnostic tools aimed at preventing severe malaria and improving the health of individuals with SCD.



Dr. Adel Driss' findings enhance the understanding of the relationship between microRNAs, SCD, and malaria.

Photos courtesy of Adel Driss

Why Ghana?

Conducting research on SCD in Ghana was essential to his study because it is a malaria-endemic country with SCD affecting approximately 2% of newborns, said Driss. (Sickle cell allele prevalence among Ghana's general population is reported to be 25%.) The West African nation's rich genetic diversity allowed him to investigate a variety of distinct sickle cell genotypes and their interactions with malaria. His project, a collaboration between Morehouse School of Medicine and the Noguchi Memorial Institute for Medical Research, has benefited the local population and also informed resource allocation in the region. "We've trained students and early-career researchers in both Ghana and the U.S.," said Driss.

Previously, Driss studied muscular dystrophies in Tunisia, France, and Japan. He's also conducted research on cancer at Emory University. "Since grad school, I've been involved in research all over the world, which is amazing and the best part of my work. I've collaborated with various institutions in different countries and trained different students at different career levels."

Sickle Cell researchers keep pace with patients as they grow beyond childhood

Until recently in Uganda, most children with sickle cell disease (SCD) never celebrated their fifth birthday—only 30% lived past this milestone. This low survival rate was mainly due to inadequate health care interventions for these children, plus lack of widespread newborn screening, explains Dr. Sarah Kiguli, a professor at Makerere University College of Health Sciences. Things are different today. Over the past decade, the East African nation has instituted a policy of screening newborns while strengthening strategies to manage their health. This means more children with SCD are growing into adolescence and adulthood.

Challenges still exist, says Kiguli. For example, the community and district facilities where many Ugandan children are born cannot provide comprehensive services, including newborn screening. Another issue: the risk of SCD complications in the kidneys, lungs, heart—in almost all organs—grows higher as patients grow older, yet scientific research in Uganda hasn't caught up with the reality of these longer lives. As a result, teens and adults with SCD don't get "the care they deserve," says Kiguli.

"It's very painful for us pediatricians to see our patients encounter challenges and problems when they transition to adult care."

Renewed research focus

Despite years devoted to children's health, Kiguli believes it's time to prioritize studies exploring appropriate SCD management for teens and adults. "We need solutions that address all the patient needs, including reproductive health, as they transition out of childhood." She's spearheaded a multidisciplinary research training program for researchers focused on the needs of people with SCD at all ages: Enhancing Research capacity for Sickle Cell Disease and related NCDs across the Lifespan in Uganda (ENRICH).

"Among our PhDs, we don't have anyone from pediatrics—and that's fine," says Kiguli. "We have someone looking at mental health in adolescence, sickle cell in pregnancy, bioinformatics, and epidemiology of malaria in SCD."

Importantly, the researchers are trained as a group to emphasize the benefits of multidisciplinary collaboration. "We've been working in silos—pediatricians alone, physicians alone, social scientists alone—that won't help us to address the comprehensive needs of these patients."

Dr. Sarah Kiguli of Makerere University leads the Fogarty-funded program: Enhancing Research capacity for Sickle Cell Disease and related NCDs across the Lifespan in Uganda (ENRICH)

Photo courtesy of Sarah Kiguli

Methodology has also been considered. "We provide both individual and team mentorship from the beginning," said Kiguli. Monthly meetings help trainees develop personal development goals and career path plans in the hopes they will continue in the field. The program also provides research training to health professionals, such as medical doctors, laboratory personnel and nurses, who are not necessarily doing degree programs—"so those who manage patients routinely might also benefit," said Kiguli.

South-to-South unity

For the project, Makerere University has partnered with Busitema University, located in eastern Uganda, where "prevalence of the sickle cell trait is as high as 20%," says Kiguli. (This contrasts with about 13% prevalence elsewhere in the country.) Studying the disease in a high burden locale is highly relevant, with results likely to influence policy and treatment guidelines.

Kiguli has other reasons for collaborating with Busitema University, which is less than 15 years old. "We want to build capacity at this young institution since our colleagues there have less chance of doing research than we do." Working and supervising trainees together will give Busitema's faculty much-needed experience, while providing faculty at both universities opportunities to learn from each other. Kiguli also hopes the new collaboration will advance progress made by their past partnerships. "Capacity must be built in a sustainable way," says Kiguli. "It's important to work collaboratively and not competitively—this is just as important for Makerere University as it is for Busitema University."

This Nigerian hematologist established an SCD stroke prevention program in the community

Sickle cell anemia (SCA) is the most severe form of sickle cell disease, an umbrella term for all disorders caused by the various sickle gene variants. Annually, more than 300,000 children worldwide are born with this inherited disease. Nigeria accounts for more than 50% of these babies. Before they reach their 20th birthday, about 11% of children with SCA will have suffered a devastating complication—stroke. As they grow older, stroke risk will increase, reaching about 24% by age 45.

In 2016, Dr. Halima Bello-Manga, a hematologist and associate professor at Kaduna State University, worked as a site investigator for a National Institutes of Health-funded clinical trial: The primary stroke prevention in children with SCA in Nigeria (SPRING). Later, she established a stroke prevention program for children with SCA at Barau Dikko Teaching Hospital, an academic facility affiliated with her university. These projects planted the seed for her ongoing Fogarty Emerging Global Leader Award study: Primary Prevention of Stroke in Children with Sickle Cell Anemia in Nigeria: Community vs Teaching Hospital.

Implementing evidence-based care

More than 20 years ago, scientists found that children who are at highest risk for stroke can be identified by measuring the velocity of blood in their cerebral vessels using Transcranial Doppler (TCD) ultrasound. Simply, high velocity corresponds to high risk. “Now, we routinely test children between the ages 2 and 16 because high-risk children can benefit from an intervention,” said Bello-Manga.

An NIH-funded clinical trial compared dosing levels of hydroxyurea for stroke prevention and found an effective lower dose, which the American Society of Hematology (ASH) also endorsed. The study also showed that twice-yearly blood tests to check for unwanted effects from this potent (and potentially toxic) drug are sufficient. Bello-Manga said, “These studies prove that it’s possible to use lower dose of hydroxyurea for stroke prevention and to administer fewer lab tests. That's a huge benefit to families because the financial burden is less.”

The three factors combined—TCD screening, hydroxyurea dosage levels, and frequency of lab testing—represent “the backbone of my project,” said Bello-Manga. She’s hoping to prove a community hospital can do as good a job as an academic hospital in correctly identifying high-risk children and managing their stroke prevention care.

Dr Halima Bello-Manga with two children (siblings with SCA) who suffered strokes before her prevention program was established.

Photo Courtesy of Halima Bello-Manga

Assistance from mentors

In Nigerian academic centers, stroke prevention teams are led by physicians, TCD is performed by radiologists, and hydroxyurea is prescribed by pediatricians or hematologists. “In our community hospital, we don’t have physicians or specialists, so we had to identify the right personnel and task-shift,” said Bello-Manga. She established guidelines so that prescribing responsibilities could be transferred to medical officers and then organized workshops—with educational videos created by her advisor, Dr. Lori Jordan of Vanderbilt University—to train nurses to perform TCD.

Her reorganization of duties proved successful, but Bello-Manga has not yet completed a feasibility study (or “non-inferiority trial”) to confirm that the community site is equal to the academic site in managing stroke prevention risk. COVID-19 disrupted her progress. “I'm behind by about one year.” Still, she’s pleased with her accomplishments so far—especially the publication of several papers.

She’s also proud to have had a profound impact on many patients’ lives. For her community program, children with SCA and stroke risk receive hydroxyurea free from the state government. Her wish is to see this replicated in all parts Nigeria and other LMICs with high burden of SCA.

As she nears completion of her project, Bello-Manga speaks with confidence about the importance of conducting sickle cell research in Nigeria. “There is nothing more interesting than observing or doing research on a certain condition in the natural space of that condition. Every patient has a different presentation and it's not what you read in books,” she said. “Our clinics are encyclopedias.”

DIRECTOR'S COLUMN

By Kathleen Neuzil, Director, Fogarty International Center

Vaccines: Potential tools for health equity

On September 9, 2024, I had the honor of (virtually) delivering the Edward Jenner Lecture for the 18th Vaccine Congress in Lisbon. Edward Jenner was an 18th century physician, who is often referred to as the "Father of Vaccinology." He pioneered the use of vaccination to control an infectious disease—specifically, he used a cowpox virus inoculation to protect against smallpox. What Jenner understood is that the two viruses, though distinct, come from the same orthopoxvirus family, and so immunization with one would protect against the other. In a treatise describing his work, Jenner wrote, "…the annihilation of the smallpox, the most dreadful scourge of the human species, must be the final result of this practice."

I received a smallpox vaccine as a child, more than a hundred and fifty years after Jenner delivered his first inoculation. Many of you reading this blog didn't receive a vaccine, because you didn't need one. Smallpox was eradicated worldwide in 1980.

My plenary talk, "Vaccines as tools for health equity," discussed the phenomenal impact of vaccination programs. Over the past half century, in addition to eradicating smallpox, vaccines are estimated to have averted 154 million deaths and saved 9 billion years of life. Here in the U.S., routine immunizations have prevented more than one million deaths and conserved an estimated $540 billion dollars over the past 30 years.

Image courtesy of the National Library of Medicine

Edward Jenner, an English physician, performed the first vaccination against smallpox in 1796.

Unfortunately, and paradoxically, global childhood immunization levels stalled in 2023. Armed conflicts and the inability to reach children are the primary cause of this drop in vaccinations. Remarkable scientific advances have catalyzed the development of new and better vaccines, yet such challenges mean that too many people do not benefit. Vaccine misinformation, vaccine hesitancy, and lack of access to vaccines have likewise contributed to the declines.

The mpox virus is an orthopoxvirus in the same family as smallpox. Mpox infections have been increasing in Africa for more than a decade. This has coincided with decreased population immunity following the discontinuation of smallpox vaccines. In 2022, mpox spread around the world and was declared a Public Health Emergency of International Concern (PHEIC). A new strain of mpox is now widely disseminated in parts of Africa, leading the WHO to declare a second mpox PHEIC in August.

Fogarty-funded public health scientists are among those leading the charge to raise awareness about mpox and to combat the outbreak in Africa. In an article published on the same day as my lecture, Fogarty grant recipient Dr. Jean Nachega and his colleagues delineate the multiple reasons why Africa, once again, must confront a public health emergency: Poverty, population displacement, lack of diagnostics, lack of vaccines… in summary, a general lack of political will. To contain the mpox outbreak, Nachega and colleagues called for long-term research investments, a leveraging of Africa's post-COVID-19 mRNA vaccine manufacturing hubs, and equitable access to diagnostics, vaccines and therapeutics. We at Fogarty are committed to scientific training and capacity building, understanding that the development of a scientific work-force will be key to preventing future pandemics and other health emergencies, while enabling a more resilient future.

Though the WHO declared an emergency in August, vaccines only reached the Democratic Republic of Congo in September, while vaccination programs only began on October 5. In contrast, mpox vaccines were widely available in the U.S. and other high-income countries during the 2022 outbreak.

I can't help but be reminded of this famous painting, "Jenner: Smallpox is Stemmed," painted by Robert A. Thom. Here, Dr. Jenner is depicted inoculating a young boy to prevent smallpox, a disease that had immense impact on children in his time. Despite the outsized effect of mpox on African children today, there's no similar picture of a child receiving a life-saving vaccine.

I can only hope that soon—more than two centuries after Jenner advanced his own dream of health equity—that new picture will be available.

PEOPLE

Abdool Karims receive Lasker Award

Quarraisha and Salim Abdool Karim have received the prestigious 2024 Lasker-Bloomberg Public Service Award. The Abdool Karims were honored for illuminating key drivers of heterosexual HIV transmission; introducing life-saving approaches to prevent and treat HIV; and statesmanship in public health policy and advocacy.

The couple helped build South Africa's scientific infrastructure and cultivated the next generation of infectious disease experts via CAPRISA (Centre for the AIDS Program of Research in South Africa), which they founded with Fogarty funding in 2002.

NIH names new AIDS research director

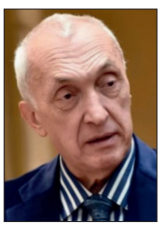
Dr. Geri Donenberg has been named the NIH associate director for AIDS research and director of the NIH Office of AIDS Research (OAR). She brings over 25 years of experience with a focus on factors that influence HIV transmission. In this role, she will lead efforts to coordinate and advance HIV/AIDS research across NIH.

Hotez to receive Winslow Award

Dr. Peter Hotez, a renowned vaccine researcher, will receive the 2024 Winslow Medal from the Yale School of Public Health for his leadership in global health, particularly his work in developing vaccines for neglected tropical diseases and codeveloping a low-cost COVID-19 vaccine, and his fight against vaccine misinformation and promoting scientific literacy.

Remembering Kawango Agot

Former Fogarty trainee and long-time grant recipient Dr. Kawango Agot has passed away. As the founder of Impact Research and Development Organization and the Nyanza Initiative for Girls' Education and Empowerment, she led nearly 60 studies and programs that shaped HIV policies in Kenya focused on women and girls living with HIV.



Tengiz Tsertsvadze dies at age 76

Dr. Tengiz Tsertsvadze, founder of the HIV/AIDS service in Georgia and general director of the Center for Infectious Pathology, AIDS, and Clinical Immunology, has died at the age of 76. Tsertsvadze, a former Fogarty trainee, was one of the main initiators of Georgia's hepatitis C elimination program.

NIAID updates mpox research priorities

The National Institute of Allergy and Infectious Diseases (NIAID) has revised its priorities for mpox research as part of the overall U.S. government. The agenda includes research into the biology of all clades (strains) of the virus; evaluating current vaccine dosing regimens; and supporting strategies for detecting the virus.

Natural antimicrobial could treat cholera

Researchers at the University of Texas at Austin explored a class of natural antimicrobials called microcins, which are produced by bacteria in the gut, and identified one that targets the bacteria that causes cholera. Microcin could potentially remove unwanted bacteria without disturbing the healthy balance of the gut microbiome.

CDC describes imported Oropouche virus infections

The U.S. Centers for Disease Control and Prevention (CDC) reported 21 imported Oropouche virus cases. Since late 2023, Oropouche virus has spread beyond the Amazon where it is endemic to new areas of South America and the Caribbean. Scientists are working to see if U.S. midge and mosquito species can carry the virus.

Marine sponge provides insights into TB

Researchers at Australia's Peter Doherty Institute for Infection and Immunity discovered a bacterium in a marine sponge with striking similarity to *Mycobacterium tuberculosis,* the pathogen that causes tuberculosis. They say their findings could inform future research and lead to the development of new TB treatment strategies, including potential vaccines.

High-risk HPV may affect male fertility

The potential effects of human papillomavirus (HPV) in men and boys are unknown. Researchers at Universidad Nacional de Córdoba in Argentina found High Risk (HR) HPV-positive men had significantly lower counts of leukocytes (a type of white blood cell) in their semen, suggesting that HR-HPV positive men could have impaired fertility.

Funding Opportunity Announcement	Deadline	Details
Global Brain Disorders Research R01 Clinical Trials Optional R21 Clinical Trials Optional	Nov 15, 2024	go.nih.gov/FogartyBrainResearch
Global Brain Disorders Research R01 Clinical Trials Optional (AIDS Research) R21 Clinical Trials Optional (AIDS Research)	Dec 9, 2024	go.nih.gov/FogartyBrainResearch
HIV-associated NCDs at LMIC Institutions R21 Clinical Trials Optional	Dec 9, 2024	go.nih.gov/HIV-NCDs

For more information, visit **www.fic.nih.gov/funding**

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In rare cases when a correction is needed after an issue's printed version has been finalized, the change will be made and explained in the online version of the article.

SCAN AND READ THIS ISSUE ONLINE

Reframing stressors of Syrian refugees

Researchers at American University of Beirut propose an innovative model for conceptualizing stressors and their impact on the mental health of Syrian refugees. Their study, funded by Fogarty and the National Institute of Environmental Health Sciences, was published in *Frontiers in Public Health* earlier this year.

Photo courtesy of Freedom House

Migrants walk on the railway tracks between Bicske and Szar, about 40 km west of Budapest, Hungary.

The number of individuals forcibly displaced has doubled over the past decade. More than 14 million Syrians have fled their homes since the beginning of the war in 2011. Adult Syrian refugees are up to 10-fold more likely to develop post-traumatic stress and other disorders than the general population of host countries. Post-displacement stressors, which include financial, political, and social components, impact Syrian refugees, sometimes "exerting a more substantial influence on mental health than war-related stressors," writes senior author Dr. Rima Habib and her colleagues. Their new study proposes a conceptual framework for how these different types of stressors contribute to survivors' outcomes.

For example, "interventions targeting one stressor can reduce the occurrence and intensity of other stressors and contribute to better mental health," state the researchers. This framework could serve as a foundation for policymakers and practitioners interested in the health and well-being of all displaced people, no matter their origins.