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GLOBAL HEALTH MATTERS

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FOGARTY INTERNATIONAL CENTER • NATIONAL INSTITUTES OF HEALTH • DEPARTMENT OF HEALTH AND HUMAN SERVICES

NIH awards help broaden climate change research

Climate change threatens human health; the complexity of its impact is enormous. In an effort to include new researchers in climate change and health (CCH) research, NIH has awarded supplemental funds to fourteen Fogarty projects.

The supplements are part of the NIH Climate Change and Health Initiative, an effort chaired by the National Institute of Environmental Health Sciences (NIEHS) that aims to reduce health threats from climate change across the lifespan. The additional funds will allow grants to add relevant metrics to their existing studies or expand their current CCH activities.

Photo courtesy of USAID in Africa

A woman and her daughter stand in a dried-out watering hole in Ethiopia.

The supplements address a broad range of topics, from the impact on land use in places like Peru (which has led to an uptick in snakebites) to effects on road safety in Ghana. All of the projects address at least one of the CCH initiative's core pillars or priority areas of science.

Advocate envisions equity for Rwandan amputees

Fogarty and the National Center for Medical Rehabilitation Research hosted a presentation by Claudine Humure, an amputee and health advocate, who discussed her plan to start a prosthetic clinic in Rwanda. Orphaned during the Rwandan genocide, Humure lost her leg to osteosarcoma at the age of 12. She was treated with chemotherapy and fitted with a prosthetic leg at Mass General Hospital in Boston a few years later with the assistance of Partners in Health (PIH). "It really felt like a privilege because I had grown up seeing many people with amputation in wheelchairs or on the streets of Rwanda," Humure recalled. "In many low- and middle-income countries people with disabilities in general, not just amputees, are excluded from any type of support or life necessities."

Photo by Fogarty International Center

Dr. Theresa Cruz (left), Director, National Center for Medical Rehabilitation Research, and Dr. Roger Glass (right), Director, Fogarty International Center, co-hosted the presentation by Claudine Humure (center). Humure plans to open a prosthetic clinic in Rwanda.

Despite improvements in the Rwandan health care system, the disability community remains at the lower rungs of society, according to Humure. Once patients have healed from their amputation, they are sent home and are seemingly forgotten. It was different for her: "PIH gave me a second chance at life. In the same way, I want to change the lives of people living with amputation in Rwanda and beyond by establishing a prosthetic center."

Her first prosthesis only lasted a year. After being unable to find a qualified prosthetist in Rwanda, she returned to Boston. That's when her journey with advanced

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FOCUS

Antivenom, an essential medicine in need of a makeover

- Catapulting antivenom into the 21st Century
- Engineering a new molecule to neutralize venoms
- Optimizing access to antivenom in the Amazon

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Fogarty program central to groundbreaking TB trial

A long-standing Fogarty-funded training partnership between Emory University and Georgian National Center for Tuberculosis and Lung Disease (NCTLD) played a critical role in the ZeNix trial testing a three-medication antibiotic regimen called 'BPaL' to treat drug-resistant tuberculosis (TB) in record time. Findings from this study, recently published in the *New England Journal of Medicine*, are expected to impact treatment protocols around the globe.

The trial, which had sites at NCTLD in Georgia, South Africa, Russia, and Moldova, shows that using half of the current recommended dose of linezolid, in conjunction with bedaquiline and pretomanid, had a success rate greater than 90 percent in treating drug-resistant strains of tuberculosis in only six months versus the nine months to two years needed for standard treatments, and with significantly lower toxicity levels for patients.

Dr. Lali Mikiashvili, a former trainee under the Emory-Georgia TB Research Training Program, was the lead principal investigator at the site in Tbilisi, Georgia, and co-authored the publication. "As someone who has worked on tuberculosis for so long, it is unbelievable to see results like this, so quickly, but the study proves that it works," she said.

Mikiashvili credits the growth in her research career to her mentors, former trainee and current MPI of the Emory-Georgia program, Dr. Nestani Tukvadze of NCTLD, and Emory's Dr. Russell Kempker, Associate Director of the Emory-Georgia TB Program, whom she met during her time training under the Fogarty program in 2017.

The Emory-Georgia TB Research Training Program was established in 2004 in response to Georgia's public health emergency due to high drug-resistant tuberculosis rates. It aims to enhance TB-related research capacity in the country through research training of Georgian investigators.

Advocate discusses vision of equity for Rwandan amputees

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prosthetic technology began. She interned with MIT's Biomechatronics Group and D-Lab, prosthesis provider Next Step Bionics & Prosthetics, and 3D design firm Autodesk while getting her bachelor's degree at Wheaton College, Massachusetts. She also worked with Boston Marathon Bombing victims at Spaulding Rehabilitation Hospital in Boston.

Humure is working toward a master's degree in Prosthetics & Orthotics at the University of Washington in Seattle with the goal of becoming a Certified Prosthetist and Orthotist because she believes, "I will be able to reach more people with this education under my belt."

Photo courtesy of Claudine Humure

Humure's high-tech prosthetic leg helped her achieve greater mobility. She hopes to bring better quality prosthesis to other Rwandans.

Theresa Cruz, Director of NCMRR, asked her, what is the greatest need for research in low- and middle-income countries?
"It is about the numbers," replied Humure. How many people are living with amputation in Rwanda, where are they located, why aren't they accessing services available to them? "If we can do more research on getting the numbers to the surface, we will educate the community, we will educate the people in power." It is necessary for stakeholders to know about the need that is too often hidden from view, she said.

While Humure's goal to start a prosthetic clinic in her home country of Rwanda is still in the ideation phase, her hope is to one day supply protheses to amputees who are unable to afford the costly ones available today. She anticipates that her work in 3D printing could help reduce the cost. She designed a 3D-printed adjustable prosthetic socket for transfemoral (above the knee) amputees, which garnered her an OZY Media Genius Award in 2017.

The center will focus on clinical care, clinical research, and continuing education and training for prosthetists and orthotists living in Rwanda with a focus on new technologies.

Humure envisions her "future prosthetic center will help restore hope and boost morale for the people living with amputation in Rwanda." She also hopes to "bring amputation data to the surface and raise the voice of the amputee community in Rwanda and sub-Saharan Africa." Director Roger Glass echoed this sentiment: "[Humure] is just the kind of person Fogarty would like to see grow and have a research center of excellence in Rwanda, with the skill set to think about frugal innovation for tens of thousands of people not only in Rwanda, but across Africa."

AFREHealth focuses on decolonization & disparities

The fifth annual AFREHealth Symposium, held in Harare, Zimbabwe, this past August, offered in-person attendance and presentations for the first time in two years. While the official theme was "COVID-19 pandemic and post-pandemic issues for health education, research, and service delivery," the topic of decolonization ran through many sessions, especially in view of the ongoing disparities brought into sharper focus by the pandemic.

Established through a Fogarty grant in 2018, the African Forum for Research and Education in Health (AFREHealth) is an interdisciplinary professional society that seeks to improve the quality of health care in Africa through research, education, and capacity building.

Photo courtesy of AFREHealth.

Francis Omaswa gave a talk entitled "Human Resources challenges and service delivery. How do we reorganize post pandemic?" at the 5th Annual AFREHealth Symposium.

Three Fogarty grantees gave plenary talks, Dr. Francis Omaswa, chancellor of Soroti University, Dr. Damalie Nakanjako, professor of medicine at Makerere University, and Dr. Catherine Kyobutungi, executive director of the African Population and Health Research Center. Dr. Ndola Prata of the University of California Global Health Institute, a consortium in Fogarty's Global Fellows and Scholars/ LAUNCH program, also presented.

"COVID should become an opportunity," to prioritize the health care workforce in Africa, said Omaswa during his talk on human resource challenges post pandemic. "Health care HR on the continent has been too focused on administrative tasks; managers don't understand the skills of their staff," he added. He stressed how the COVID-19 pandemic exacerbated worker shortages in all countries, but especially in lower income ones as higher-income countries could recruit from abroad to deal with the patient influx.

"If Africa doesn't employ our own healthcare workers they will be 'taken' by the Global North," Omaswa warned. His recommendations included African nations investing in their health workforce; development and support of national health resource plans; coordination between government, academia, and the private sector; and standardizing competencies for health care workers to bring about clinical excellence.

In her talk, Kyobutungi focused on reframing global health from a paradigm that sees part of the world (usually the Global South) as having problems and the other part (the Global North) as having solutions to one in which both problems and solutions are defined collaboratively. This was echoed by Ndola Prata who championed transitioning from "capacity-building" to "capacity-bridging"– acknowledging the capacity that exists within Africa.

This was also the first in-person conference since the loss of two AFREHealth leaders—Drs. James Hakim and David Olaleye. Both died from COVID-19 in 2021. Hakim was a member of the AFREHealth governing council and Olaleye oversaw AFREHealth's symposium in 2019. Both were involved in the Medical Education Partnership Initiative (MEPI) program, one of the progenitors of AFREHealth. Fogarty Director Roger I. Glass paid tribute to both men in his remarks during the opening plenary session: "James and David were both profoundly important leaders in advancing medical research and education in Africa. My hope is that their work will inspire a new generation to dedicate themselves to improving health on the continent."

Webinar series highlights food insecurity

Fogarty's Center for Global Health Studies is hosting a three-part webinar series on Global Food and Nutrition Insecurity.

The series will highlight innovative research projects on nutrition, food insecurity, and health outcomes as well as opportunities for adaption in the U.S.

All times Eastern Time

- **Nov. 3 at 10 a.m.** – Overview of Global Food and Nutrition Insecurity
- **Nov. 10 at 10:30 a.m.** – Leveraging Food Environment for Food and Nutrition Security
- **Nov. 21 at 3 p.m.** – Using Implementation Science to Address Food and Nutrition Insecurity

PROFILE

Improving the oral health of Kenyan teens living with HIV

People living with HIV/AIDS often experience oral health issues, including tooth decay, painful sores and blisters, and periodontitis (bone loss around the teeth). Antiretroviral therapy (ART), a form of HIV treatment, has made these problems less common yet the medications themselves sometimes cause dental side effects. The Children's HIV Oral Manifestations Project (CHOMP) is examining the relationship between oral disease, saliva, blood levels of vitamin D, and a patient's overall quality of life.

Ashley Karczewski joined CHOMP to better understand these complex oral dynamics in teens affected by HIV in Kenya, home to approximately 150,000 children living with HIV/AIDS. "Oral manifestations of HIV can greatly impact quality of life for these children. If they have tooth pain, they miss school. Sometimes malnutrition results if they lose teeth or have trouble chewing," said Karczewski. For her Fogarty project, she focused on levels of antimicrobial peptides (AMPs) found in saliva that are protective of oral health.

Microbes in our mouths

Our mouths are home to between 300 and 700 different bacterial species and our saliva contains AMPs that modulate this thriving community of organisms. AMPs benefit our health by boosting immunity and helping to prevent oral disease.

"What we found was that there was a correlation between the vitamin D status of the children and the salivary AMP cathelicidin LL-37—but it was the opposite of what we'd anticipated," said Karczewski. Children with adequate vitamin D status had less, not more LL-37. The team's theory is that vitamin D is a precursor to LL-37. So children with more LL-37 may have expended more vitamin D to produce their high levels of the beneficial AMP. "We also found a correlation to the ART regimen," said Karczewski. "Children who began receiving ART earlier in life had higher levels of LL-37 and another AMP. So that means ART was likely helpful in boosting their immune systems."

CHOMP, a collaboration that began four years ago between the University of Washington and the University of Nairobi, continues working towards its aims.

Ashley Karczewski, DDS

Fogarty Fellow: 2019-2020

U.S. institution: Indiana University (Northern Pacific Global Health Consortium)

Foreign institution: University of Nairobi School of Dental Sciences, Kenya

Research topic: Oral health in children living with HIV

"The goal is to gather data and then do a big clinical trial, where we provide vitamin D supplementation as a way of boosting the innate immunity of children living with HIV." The trial should begin in about two to three years and, if the results are beneficial, a similar cost-effective vitamin D supplementation plan "can be applied in other nations, whether low, middle or high income," said Karczewski. "Because cancer, diabetes, hypertension and other health issues create a compromised oral environment, vitamin D supplementation would be helpful to many people." Currently, the CHOMP team is preparing to publish a series of papers analyzing their results.

Karczewski received instruction on research methodology, grant and paper writing, and Institutional Review Boards (IRBs) through her fellowship. "One positive of the pandemic is it allowed me to focus on writing and career development," she said. "We had bi-weekly consortium calls to discuss different topics and to hold workshops on grant and paper writing. Previously I'd done only bench research so this was like a PhD-lite year for me." The disruption caused by SARS-CoV-2 also taught her "resiliency in the face of dealing with the limitations of a global pandemic. I was working with a huge team and coordinating between all these different people and moving parts." Her Kenyan and U.S. mentors provided much-needed guidance.

Since her Fogarty Fellowship, Karczewski has finished dentistry school and begun a residency in a cancer center. "What I learned in Nairobi helped me with all my patient interactions and also with my focus on medically compromised people." Karczewski credits Fogarty with guiding her towards a career in hospital dentistry and clinical research. "I'm focused on cancer in my residency so I'm hoping that becomes my research niche— dentistry for cancer patients in a global health setting."

Q&A

JENNIFER WEBSTER-CYRIAQUE, DDS, PHD

Dr. Jennifer Webster-Cyriaque, deputy director of the National Institute of Dental and Craniofacial Research (NIDCR), earned her DDS from SUNY Buffalo and her Ph.D. in microbiology/immunology from the University of North Carolina (UNC)-Chapel Hill. She served on the faculty at the UNC schools of dentistry and medicine for more than two decades. Her research has explored causes for salivary gland disease in patients living with HIV and evaluated the oral microbiome's impact on cancer-causing viruses and HIV outcomes. Since 2004, she's led the UNC-Malawi project, which helped establish that nation's first dental school in 2019.

What inspired you to become a scientist?

As a child, I was always a very curious person, but I never entertained being a scientist because I didn't really have an example. The one person I was aware of was George Washington Carver, and then my older sister became a nurse, so I decided I would do something health related.

At college, I focused on becoming a doctor but then I read "The Unkindest Cut" by Marcia Millman and I recognized I would not be a good person to tell someone their loved one is dying or "we don't know what to do." So, I started to look for other professions and did a lot of volunteering and work study. One job, cleaning dishes in the laboratory, included some science project work during the summer and a volunteer position with a dentist in Buffalo led to a dental assistant's job. That's when I discovered that I really liked dentistry.

What do you enjoy most about your work?

I enjoy seeing patients. It's like Christmas when you deliver new dentures to someone or when you relieve their pain. There's a win in that. But at the same time there's huge gratification in what you learn at the bench and take back to a patient—this is why my career has progressed on parallel tracks.

For me, science is a tool. I used to believe that scientists were these [she gestures indicating a person standing on a pedestal]. But now I realize that everybody who asks a question is a scientist—a scientist is somebody who really wants to know the answer.

What should we know about oral health?

Oral health is essential and can be the genesis of other health problems, yet it has been overlooked. Think about it: your communication, your nutrition, your portal to every other organ is your mouth, yet oral health has mainly been touted as white teeth. They are pretty and what you show the world is important, but there's so much more there, right? Oral health is a barometer for what's happening elsewhere in your body. If you take saliva, you can measure many diseases at distant sites. Who wouldn't want to give spit instead of getting a needle? It's easier and safer.

Oral cancers are a major problem. Virus-associated cancers cause more than 70% of head and neck cancers in the U.S., which is more than tobacco- or alcohol-related cancers. One challenge for our field—and this is something we're working on—is building the evidence base with large enough studies to be able to demonstrate linkages to various diseases. I think as those studies grow, we will be able to see many direct connections, just as we've seen between oral health and cardiovascular disease.

What do you hope to accomplish at NIH?

The most common disease in the whole world is tooth decay (dental caries), which is preventable. This past December, the Oral Health in America report clearly showed that disparities remain a major issue, despite technological advances. So, I would like to address disparities nationally and globally. Part of that is getting prevention messaging out there and helping to build capacity.

We need to integrate oral and general health; we need to diversify the workforce so that dentists look like the populations they treat; and we need to translate and implement what we've learned through research, because so much of what we know has never made it to the patient. As NIDCR's deputy director, my potential impact is much larger now. Beyond a single patient or small group, I will be able to make programmatic changes, promote other people's science, and help build training programs across the nation. Alongside Fogarty, I hope to make a difference globally as well.

Catapulting antivenom into the 21st Century

In 2018 the World Health Organization proposed a strategy for reducing, by half, the mortality and disability caused by snakebites by the year 2030. Key to this plan is "ensuring safe, accessible and effective treatment."

While an effective treatment—antivenom—currently exists, Constantinos Kurt Wibmer believes it can be improved and made more accessible. "Antivenom works but it has some of the same problems as all other medicines in low- and middle-income countries (LMICs): it's expensive and in short supply," said the virologist and structural biologist at the University of the Witwatersrand's Wits Health Consortium in South Africa. Add in the need to keep antivenom at low temperatures and the possibility of extreme side effects due to impurities and "safe, accessible, and effective" looks less achievable. "If we had a modern drug, we would be able to get around these issues. For example, we can make something that's temperature stable. We can make something that's pure, so you can avoid anaphylactic shock. We might even be able to make compounds that can be given in the field instead of rushing someone to a hospital to give antivenom by IV," said Wibmer.

Reducing death and disability caused by snakebite

Scientists believe five million snakebites occur each year, yet this number is likely inaccurate due to underreporting. Roughly half a million annual bites are serious leading to between 100,000 and 150,000 deaths. The remaining 400,000 people will lose an arm, a foot, or maybe an eye, said Wibmer: "So that's a livelihood gone—if you can no longer work in the field or you can't walk because your foot

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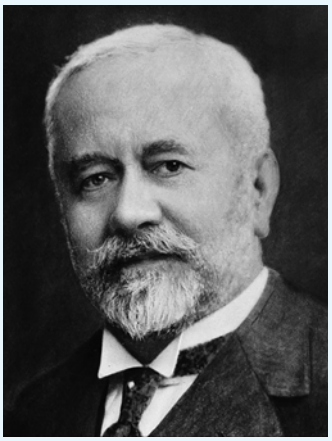
A brief history of antivenom

Antivenom (also referred to as "antivenin") is an antibody therapy that can disable the toxins within a specific venom if injected quickly into a patient after a bite. French scientist and physician Albert Calmette is credited with creating the first snake antivenom.

Over more than 120 years, production of antivenom, which must be tailored to species of snakes, remains much the same. Most antivenoms are produced in horses, some in sheep; a small amount of venom is injected into the animal, causing an immune system reaction and release of antibodies, which are later harvested via bleeding. This blood plasma is then concentrated and purified into pharmaceutical grade antivenom.



Albert Calmette, Scientist & Physician

While the basic production method has remained little changed, many technological advances and purification processes have been introduced to achieve higher quality products and reduce side effects. Additionally, in the 1970s, antivenom began to be administered via the intravenous route (injected into the vein) as opposed to the subcutaneous route (injected under the skin) or intramuscular route (injected into the muscle). This has helped decrease severe reactions.

By the end of the 20th century, antivenom manufacturers began to dwindle worldwide, due to complexity of production, high production expenses, and lack of a lucrative market. This has resulted in a dramatic increase in the price of some products over the last two decades. Antivenom availability has also declined significantly. Meanwhile untested, unethically produced, or fake products have entered the market. The populations hardest hit by shortages of antivenom, which is included on the WHO's List of Essential Medicines, live and work in rural areas of less-developed nations where highly venomous snakes are endemic.

Experts in the field suggest these changes to help increase antivenom supply: establish production in developing countries (following the example of Brazil's Instituto Butanan); introduce new methodologies to reduce costs while further increasing the quality of products; and apply state-of-the-art technologies to abolish the use of animals in anitvenom production.

has been amputated. And that will affect the whole family and possibly an entire community."

Hundreds of snakes are responsible for bites with up to 200 that can "really do damage," said Wibmer. Each snake acts on its prey in a different way so different venoms have unique components; this also means patients must correctly identify a snake to receive the correct antivenom. For example, the venom of certain vipers or adders common to South and Central Americas and Central Africa affects how blood clots, leading to bleeding from the eyes. Other venoms can spur a blood clot leading to a heart attack or an embolism.

"Then the neurotoxic snakes, like cobras and mambas, can shoot venom into your eyes, where it goes straight to the nervous system, slowing down breathing and heart rate."

> "We can make something that's pure, so you can avoid anaphylactic shock. We might even be able to make compounds that can be given in the field instead of rushing someone to a hospital to give antivenom by IV."

Years of experience in virology showed Wibmer how antivenom can be transformed. Next-generation antivenoms need to be "high-affinity products that are long-lasting in the body, which is what we engineer into current therapeutics for other diseases," he said.

Wibmer is pursuing two different approaches to achieve these goals. "One is the antibody isolation approach—trying to get antibodies from immunized animals and then making them in a lab, so that they can be 100% pure, engineered to stay in the body for a month, and effective in a small enough dose to be given in the field," he said. A second approach is based on structural biology methodologies: Identify proteins that resemble the targets of venom (such as blood clotting cascades) and then enhance them through engineering.

Wibmer uses both approaches in his efforts to synthesize a broadly reactive therapeutic for various snake species native to both Africa and Asia. He has expressed snake toxins from each of the major toxin classes and characterized them using x-ray protein crystallography.

Constantinos Kurt Wibmer believes antivenom can be improved. His experience working on therapeutics for HIV informs his current work.

Photo courtesy of Constantinos Kurt Wibmer

The next step in his project is to use structure-guided protein design to improve the binding regions of his lead protein candidates. So far he's built "a solid foundation" for continued work, despite disruptions caused by SARS-CoV-2. "Africa has huge shipping issues, which the pandemic exacerbated. I am now receiving things that I ordered in 2020!"

Wibmer remains hopeful of a good result because venom is unlike his former research focus, HIV, which is a "moving target" that evolves in millions of people every year. "Snakes evolved venom for their prey—they do not care about humans—so it's the same toxin honed for the same rodents and birds. Even though venoms are diverse, it is easier to design interventions for them, because they're a stable target." Still he does not underestimate the challenges he faces, such as disseminating new medicines to LMICs and getting interest from Western pharmaceutical companies or investment for local drug development and manufacturing.

"A lot of people in LMICs don't think highly of their own science. They think science is not important unless it comes from one of the big Western countries. When you look at the big labs doing work in India, in Africa, in Brazil, the people are comparable but getting them to believe that they are just as good as 'big name so and so' presenting at the conference—this is something we need to address. Because that confidence helps drive the passion and inspires people to produce good science."

Engineering a new molecule to neutralize venoms

Claire Komives, a professor of chemical engineering at San Jose State University, California, also works to modernize antivenom, yet her approach is unlike that of Constantinos Kurt Wibmer *(see story, page 6)*. She entered this field after reading a news article around the time she was taking a sabbatical year at the Indian Institute of Technology, Delhi. The article falsely claimed that a particular opossum peptide could neutralize venom from several different snakes. "The data was terrible, still it got me thinking." After all, she knew that when an American rattlesnake bites an opossum, the animal simply licks its wounds and moves on.

"Just for the heck of it, I purchased some synthesized opossum peptide and sent it to the National Natural Toxins Research Center at Texas A&M University in Kingsville, and they tested it and found that it indeed neutralized a lethal dose of rattlesnake venom." Excited, Komives began to compose her wish list for a next generation antivenom: heat resistant, shelf stable, available as a either pill, liquid, or inhalable mist, and, of course, "super inexpensive."

Working with India and Nigeria

India is thought to have the highest loss of life due to snakebites in the world. A 2020 study estimated 58,000 deaths each year in the country. Komives estimates that areas of Nigeria likely "have equal snakebite prevalence as India," while the WHO recorded 6,687 people treated for snakebite envenoming in a single Nigerian hospital over a three-year period. Her research has led her to work in both countries.

The king cobra, the largest of venomous snakes, is found predominantly in forests from India through Southeast Asia. Their venom is neurotoxic.

Public domain

The team on her project in India, funded by the National Institute of Biomedical Imaging and Bioengineering, ran experiments "to determine whether the peptide, in its native form, could actually serve as an antivenom—meaning you inject it and it'll work." The tests showed the molecule, in itself, did not work as antivenom, yet she had gained knowledge about its characteristics, including how it binds to other molecules. Seeing an active site, Komives decided to "try to display the peptide the way the serum protein in the opossum does." She attached the peptide to a camelid nanobody, a technique increasingly used in pharmacology, and now it can be expressed in *E. coli*.

India is thought to have the highest loss of life due to snakebites in the world. A 2020 study estimated 58,000 deaths each year in the country.

Her rejiggered molecule works to neutralize venom "for almost all the Nigerian snakes and one Indian snake, the saw-scaled viper," said Komives. Currently, she is working on creating a process to produce an active protein that scales in *E. coli*. "If it's successful, then we're talking about having a cheap, single molecule antivenom" that could undergo robust "lot by lot quality control," she said.

Komives's progress, like Wibmer's, has been delayed by world events. "During the pandemic we weren't allowed to come to the lab, and then it took six months to get a certain part for my bioreactor." Yet her efforts to design an antivenom continue.

Komives is currently working with the Ministry of Health in Nigeria to do "preliminary safety and efficacy tests, which would be the next step to making the peptide commercialize-able." Her project has also found support in India, where current manufacturing methods (that use horses) are seen as unethical.

"The Nigerian hospital I'm working with sees 3,000 snakebite patients each year, mostly in the rainy season," she said. Yet, the antivenoms available there are insufficient and cost $100 a dose. "These rural farmers in Nigeria, they simply don't have the money. They are destroyed financially if somebody in the family gets bit."

Optimizing access to antivenom in the Amazon

The current generation of antivenoms may be imperfect, still they are an "efficacious and extremely safe" therapy for snakebite, said Dr. Charles Gerardo, a professor and emergency medicine specialist at Duke University. "Yet antivenoms are not getting into people—if no one ever sees antivenom in a timely fashion due to travel times, lack of infrastructure, lack of knowledge, then it does no good." Gerardo has been conducting a study to improve antivenom access and distribution in Brazil, the results of which he hopes can be applied in other regions in the world.

Over the past five years, Brazil recorded roughly 140,000 cases of snakebite. Of these, about 70,000 resulted in death or illness. One aim of Gerardo's project is to create a distribution model for antivenom, which is state produced at Instituto Butantan, using Brazil's existing network of community health centers (CHCs) embedded within its nationalized health care system. Joao Ricardo Vissoci, co-investigator and an assistant professor at Duke, explained, "The data showed a majority of snakebite events in the Amazon do receive antivenom, but a large proportion are delayed—meaning outside the six-hour window." (There's a greater likelihood of death or lasting effects when patients receive antivenom more than six hours after a bite.)

A crucial parameter in creating a distribution model, then, is the ability for most of the at-risk population to be able to travel to an antivenom site within six hours of a bite. Addressing this, the team, which includes Brazilian colleagues at the Tropical Medicine Center in Manaus, Amazonas, mixed "implementation science with data science," said Vissoci.

Progressive methods to find solutions

Gerardo explained: "We took satellite imagery to find man-made structures and attributed populations to those areas. Then we had to determine travel times." Given most people in the Amazon travel by river, the team created datasets of the entire river basin at two different times of the year—during the wet season and the "wetter" season. "Once we modeled where the people are and how long it would take to get them to care," said Gerardo, "then we could begin to generate location allocation plans—which CHCs do we (stock with antivenom) based on this data?"

Next, the team piloted a training process for teaching community health workers how to administer antivenom, including identifying types of snakebite, dealing with allergic reactions, and when to transfer a patient to a higher level of care. The team also established clinical practice guidelines and minimum requirements for individual CHCs to qualify for administering antivenom. Finally, the team conducted various cost-effectiveness analyses, which showed that providing treatment at CHCs reduces hospital use and gets antivenom into patients faster.

While most people bitten by poisonous snakes in the Amazon, like this cotton mouth viper, receive antivenom, it is often administered past the recommended six-hour window.

Courtesy of Charles Gerardo

Meeting the 2030 WHO goal

"If we continue on this path, we are on track to meet the 2030 WHO goal of reducing death and disability by snakebite in Brazil," said Vissoci. Brazilian by birth, he said it is essential to build bridges across institutions and countries to contribute to global health. "We should be leveraging data better in the low-income world, because it takes a lot of work for people in these countries to generate that data. The computing capacity Duke has, including cloud computing data science techniques, means I can deploy artificial intelligence in the Amazon to understand how to distribute healthcare resources."

While the global pandemic impacted the project, the team "navigated COVID pretty well," said Gerardo, noting "a lot of this work involved advanced geospatial (analysis) and artificial intelligence and used existing data. We overcame challenges by being innovative." The team remains on track and now most of the work is "in the manuscript or presentation phase, which is where we should be right now."

OPINION

By Dr. Roger I. Glass, Director, Fogarty International Center

Oral health researchers welcome here!

I was thrilled to give the keynote address at the annual meeting of the International Association for Dental Research. A renewed sense of urgency in global oral health is surfacing now and highlighted by two recent publications. One is the recent *Lancet* Commission on Oral Health, which brought together a collection of world-renowned experts to consider the opportunities and challenges ahead, primarily in the areas of global access to care and delivery. The second is the 2021 WHO Draft Global Strategy on Oral Health that has presented a fresh plan for tackling oral diseases. The WHO proposal includes a framework for tracking progress with measurable targets to be achieved by 2030.

There is a growing recognition that oral health has been left out of the agenda for universal health care (UHC). We all recognize that it's impossible to exclude dental health from general health. It follows, then, that UHC can only be achieved when oral care is included in the commitment to "better health for all."

I believe medical research and oral health research need not be conducted in silos. We at Fogarty welcome bright ideas from anyone from any discipline seeking to work on oral health issues. I see an abundance of opportunities spanning diverse medical and dental interests.

Though only a small percentage of NIH's $45 billion dollar budget goes directly to Fogarty's international agenda, all the institutes maintain global footprints, while more than half have joined us to fund global health projects.

Currently, the NIH has the good fortune of outstanding senior leadership with deep roots in oral health. Dr. Lawrence Tabak, is currently performing the duties of the NIH Director after previously holding the post of director of the National Institute of Dental and Cranial Research (NIDCR). Meanwhile, the NIDCR's current director, Dr. Rena D'Souza, has strongly supported and promoted global oral health throughout her tenure.

The recent appointment of Dr. Jessica Webster-Cyriaque as NIDCR's deputy director also speaks to an international vision. Webster-Cyriaque helped found a training program in Malawi as well as that nation's first dental school *(see this issue's Q&A on page 5).*

Fogarty's portfolio develops talent by sponsoring qualified, emerging investigators and giving them protected time to conduct research in LMICs. Individual research opportunities include one-year fellowships for students and postdocs from anywhere in the world. While still a dental student, Dr. Ashley Karczewski, helped conduct a survey of the provision of oral health care to teens living with HIV in Kenya as her Fogarty project. Past dental fellows include Dr. Lilliam Pinzon, who evaluated dental restorations in underserved HIV-positive children in Mexico.

Another Fogarty program, the International Research Scientist Development Award, provides five years of mentored support for U.S. postdoc scientists who wish to spend 50% of that time in an LMIC. Meanwhile, the Emerging Global Leader Award offers the same level of support for postdoc scientists from LMICs. Fogarty has supported Dr. Lord Gowans, who used genomic sequencing to elucidate the etiology of cleft palate in Ghana, and Dr. Dalton Wamalwa, who created an oral health training program called TABASAMU—a Swahili word meaning "smile"—for dentists wishing to work with HIV/AIDS patients in Kenya.

Two additional Fogarty programs, Data Science for Health Discovery and Innovation in Africa (DS-I Africa) and Mobile Health: Technology and Outcomes in Low and Middle Income Countries (mHealth) also welcome scientists with original oral health research projects.

Regarding mHealth, I wonder: What conditions could smart phone images help detect in the face, mouth, jaw, and gums? Could a mobile phone equipped with AI help diagnose patients who are supported by community health workers?

This is an extraordinary time to expand and articulate Fogarty's global training and research agenda in the area of oral health. It will always be our mission to seek fresh scientific minds and projects committed to the goal of radical inclusion: better health, including oral health, for all.

PEOPLE

Fauci to step down

After 54 years of public service at NIH, Dr. Anthony Fauci, Director of NIAID and Chief Medical Advisor to President Biden, announced he will be stepping down in December 2022. Fauci served as NIH's face for many infectious disease threats during his decades-long career, including HIV/AIDS, West Nile virus, Ebola, Zika, and COVID-19.

Barbosa da Silva Jr. to lead PAHO

Dr. Barbosa da Silva Jr. was elected Director of the Pan American Health Organization (PAHO) during the 30th Pan American Sanitary Conference in September. Dr. Barbosa da Silva Jr. will begin his tenure in February. Currently the Assistant Director at PAHO, he was previously Brazil's Secretary of Health Surveillance.

Nkengasong awarded Virchow Prize

PEPFAR Ambassador Dr. John Nkengasong has received the prestigious Virchow Prize for his long career of trailblazing contributions to global health. The prize recognizes the lifetime achievements of those dedicated to improving the health and well-being of the world's most vulnerable and whose accomplishments align with the United Nations Sustainable Development Goals (UN SDGs).

Former Fogarty scientist heads Pasteur Network

The Pasteur Network has named Dr. Rebecca F. Grais, a former Fogarty scientist, Executive Director. The network brings together 33 institutions to improve human health through biomedical research, public health activities, training, and innovation. Grais has extensive experience in epidemiological research focused on underserved populations.

Fogarty-funded research receives AAAS award

An inexpensive paper microscope called the Foldscope received a 2022 Golden Goose award from the American Association for the Advancement of Science. Support from NIH was foundational to the early research that went into its creation. Co-creator Dr. Manu Prakash first conceived of a cheap microscope while studying malaria in Thailand.

Dr. Jim Cybulski was a student in Prakash's lab at Stanford University when he started working with Dr. Prakash on the Foldscope. He also helped field test the microscope in Southeast Asia and Africa. The award recognizes federally funded science that has led to breakthroughs in biomedical research, medical treatments, and computing and communications technologies.

Global HEALTH Briefs

New guidance promotes equitable research partnerships

The ESSENCE on Health Research initiative & UK Collaborative on Development Research published a Good Practice document laying out four interconnected approaches to supporting equitable partnerships in global health research. Fogarty is a member of ESSENCE and contributed to the document which draws on the experience of funders, research organizations, and researchers in low-, middle- and high-income countries.

PIH establishes Farmer Scholarship Fund

Partners In Health announced a new $200 million scholarship fund named for the late humanitarian, physician, and global health advocate Paul E. Farmer. The fund will support medical students and global health delivery master's degree candidates at the University of Global Health Equity (UGHE) in Rwanda for the next 25 years.

CUGH launches capacity platform

CUGH released its new Capacity Platform with the goal of connecting trainers with the training needs of institutions in low-income countries. It also allows institutions as well as affiliated individuals to post their training needs and training offerings, and users to search implementation science listings separately from general ones.

USAID announces TB elimination project

Supporting, Mobilizing, and Accelerating Research for Tuberculosis Elimination (SMART4TB) is a five-year initiative that will invest up to $200 million to identify more effective methods and tools for finding, treating, and preventing tuberculosis in 24 priority countries via an international consortium in the U.S., South Africa, India, Uganda, Kyrgyzstan, and Vietnam.

US and WHO hold Strategic Dialogue

HHS Secretary Xavier Becerra and WHO Director-General Dr. Tedros Adhanom Ghebreyesus, along with representatives, met in September to discuss priority global public health issues, areas of collaboration, efforts to develop a new pandemic instrument, and strengthening the International Health Regulations (IHR). The next Dialogue is slated for late 2023.

Funding Opportunity Announcement	Deadline	Details
Emerging Global Leader K43 Independent Clinical Trials Required K43 Independent Clinical Trials Not Allowed	Nov 3, 2022	http://bit.ly/E_Lead
Global Brain Disorders Research R21 Clinical Trials Optional R01 Clinical Trials Optional	Nov 15, 2022	http://bit.ly/NIHGlobalBrain
HIV-associated NCDs Research at LMIC Institutions R21 Clinical Trials Optional	Dec 8, 2022	https://bit.ly/HIV-NCD
Global Brain Disorders Research (AIDS) R21 Clinical Trials Optional R01 Clinical Trials Optional	Dec 9, 2022	http://bit.ly/NIHGlobalBrain

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

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Tracking equity through authorship

The percentage of Fogarty-funded publications about the SSA region featuring SSA-affiliated first and/or last authors increased by over 15% between the years 2008 and 2020.

Image courtesy of Ezinne Akudinobi and Peter Kilmarx

It matters—greatly—when a published study about sub-Saharan Africa credits scientists from the region as first or last authors. Authorship not only indicates leadership in conducting and sharing research, it also is an essential part of a researcher's career. Good news: The number and percentage of Fogarty-funded publications about the region with sub-Saharan Africa (SSA)-affiliated first and last authors increased between the years 2008 and 2020, according to a new Fogarty-authored study published in *BMJ Global Health*.

"While SSA makes up 12.5% of the global population, only 1.1% of the world's researchers are based in the region," wrote Fogarty co-authors Ezinne Akudinobi and Deputy Director Dr. Peter Kilmarx. In addition to the total number of publications from the region rising, the percentage of those authors with an SSA affiliation rose as well – from 45% to 63% for first authors and 28% to 46% for last.

What's needed is an investigation of impediments faced by SSA authors—language barriers, stringent authorship guidelines, and editorial bias, among them. "There is more at stake than publish or perish," concluded Akudinobi and Kilmarx. "Ideally, African authorship will increasingly reflect Africans setting research agendas and writing about African issues for African audiences."