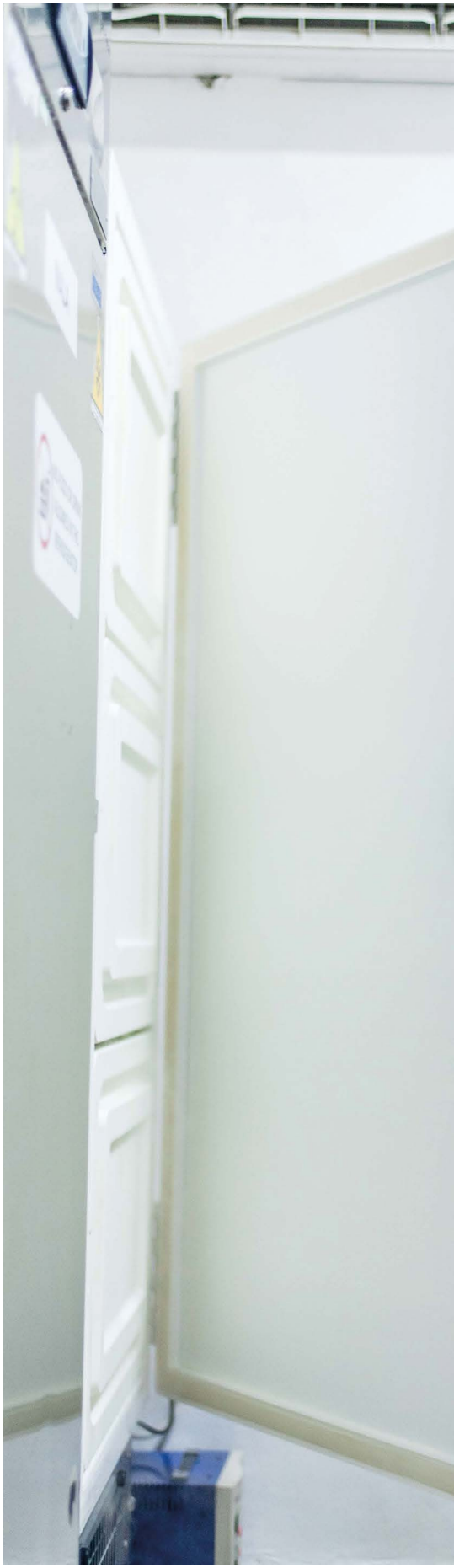


THE NEXT CHAPTER FOR AFRICAN GENOMICS

Nigeria is poised to become a hub for genetics research, but a few stubborn challenges block the way.

By Amy Maxmen

In the affluent, beach-side neighbourhoods of Lagos, finance and technology entrepreneurs mingle with investors at art openings and chic restaurants. Now biotech is entering the scene. Thirty-four-year-old Abasi Ene-Obong has been traversing the globe for the past six months, trying to draw investors and collaborators into a venture called 54Gene. Named to reflect the 54 countries in Africa, the genetics company aims to build the continent's largest biobank, with backing from Silicon Valley venture firms such as Y Combinator and Fifty Years. The first step in that effort is a study, launched earlier this month, to sequence and analyse the genomes of 100,000 Nigerians.

At a trendy African fusion restaurant, Ene-Obong is explaining how the company can bring precision medicine to Nigeria, and generate a profit at the same time. He talks about some new investors and partners that he's not able to name publicly, then pulls out his phone to show pictures of a property he just purchased to expand the company's lab space.

"My big-picture vision is that we can be a reason that new drugs are discovered," Ene-Obong says. "I don't want science for the sake of science, I want to do science to solve problems."

It's too soon to say whether he will succeed. But his ambitions would have been unthinkable a decade ago, when most universities and hospitals in Nigeria lacked even the most basic tools for modern genetics research. Ene-Obong, the chief executive of 54Gene, is riding a wave of interest and investment in African genomics that is coursing through Nigeria. In a rural town in the western part of the country, a microbiologist is constructing a US$3.9-million genomics centre. And in the capital city of Abuja, researchers are revamping the National Reference Laboratory to analyse DNA from 200,000 blood samples stored in their new biobank. Studying everything from diabetes to cholera, these endeavours are designed to build the country's capabilities so that genetics results from Africa — the publications, patents, jobs and any resulting therapies — flow back to the continent.

The rest of the world is interested, too. Africa contains much more genetic diversity than any other continent because humans originated there. This diversity can provide insights into human evolution and common diseases. Yet fewer than 2% of the genomes that have been analysed come from Africans. A dearth of molecular-biology research on the continent also means that people of African descent might not benefit from drugs tailored to unique genetic variations. Infectious-disease surveillance also falls short, meaning that dangerous pathogens could evade detection until an outbreak is too big to contain easily.

54Gene aims to create Africa's largest biobank.

But Nigeria's genetics revolution could just as soon sputter as soar. Although the country is Africa's largest economy, its research budget languishes at 0.2% of gross domestic product (GDP). Biologists therefore need to rely on private investment or on funding from outside Africa. This threatens continuity: one of the largest US grants to Nigerian geneticists, through a project known as H3Africa, is set to expire in two years. There are other challenges. Human research in Africa requires copious communication and unique ethical consideration given the vast economic disparities and history of exploitation on the continent. And a lack of reliable electricity in Nigeria hobbles research that relies on sub-zero freezers, sensitive equipment and computing power.

Yet with a hustle that Nigerians are famous for, scientists are pushing ahead. Ene-Obong hopes to pursue research through partnerships with pharmaceutical companies, and other geneticists are competing for international grants and collaborations, or looking to charge for biotech services that are usually provided by labs outside Africa. Last November, Nnaemeka Ndodo, chief molecular bioengineer at the National Reference Laboratory, launched the Nigerian Society of Human Genetics in the hope of bringing scientists together. "When I look at the horizon it looks great — but in Nigeria you can never be sure," he says.

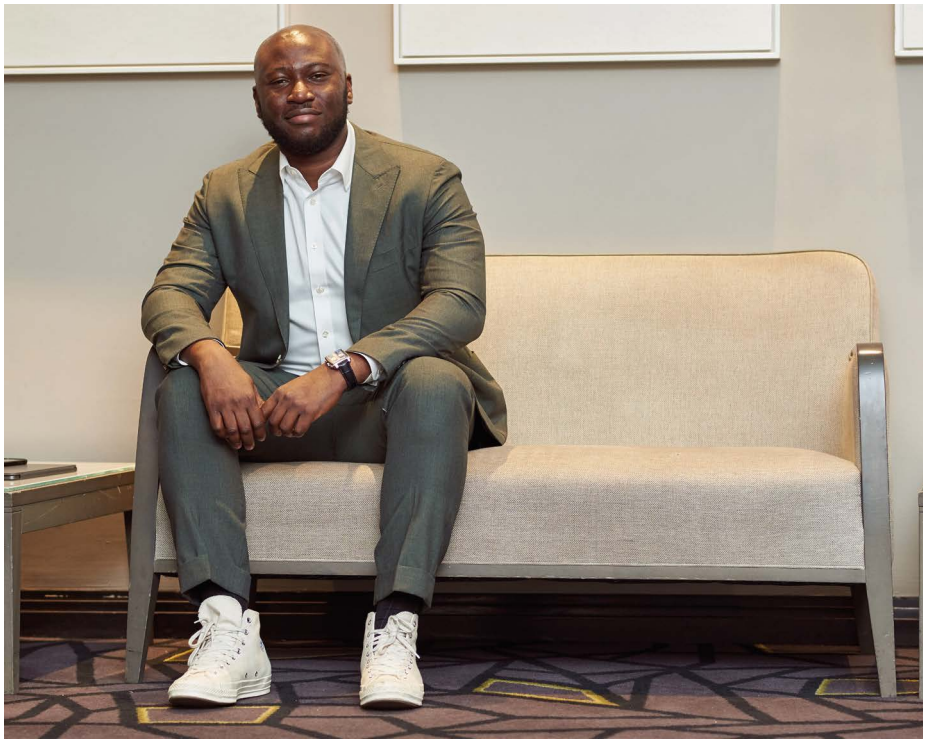
Building the foundation

Around 15 years ago, Nigerian geneticist Charles Rotimi was feeling dismayed. He was enjoying academic success, but would have preferred to do so in his home country. He had left Africa to do cutting-edge research, and he was not alone.

Many Nigerian academics move abroad. According to the Migration Policy Institute in Washington DC, 29% of Nigerians aged 25 or older in the United States hold a master's or a doctoral degree, compared with 11% of the general US population.

After Rotimi joined the US National Institutes of Health (NIH) in Bethesda, Maryland, in 2008, he hatched a plan with director Francis Collins to drive genetics research in Africa. Rotimi wasn't interested in one-off grants, but rather in building a foundation on which science could thrive. "The major thing to me was to create jobs so that people could do the work locally," he says. In 2010, the NIH and Wellcome, a biomedical charity in London, announced the H3Africa, or Human Heredity and Health in Africa, project. It's become a $150-million, 10-year initiative that supports institutes in 12 African countries. The proof of its success will be not in the number of papers published, but rather in the number of African

54GENE



54Gene chief executive Abasi Ene-Obong is preparing to make Nigeria a genetics powerhouse.

investigators able to charge ahead after the grant ends in 2022.

For that to happen, H3Africa researchers realized they needed to revise research regulations and procedures for gaining the public's trust. So rather than just collecting blood and leaving — the approach disparagingly referred to as helicopter research — many investigators on the team have devoted time to adapting studies for the African context.

For example, when Mayowa Owolabi, a neurologist at the University of Ibadan, Nigeria, was recruiting healthy controls for his H3Africa study on the genetics of stroke, his team discovered that many people had alarmingly high blood pressure and didn't know it. Nigeria has one of the world's highest stroke rates, and Owolabi realized that communities needed medical information and basic care more urgently than genetics. So he extended his study to include education on exercise, smoking and diet. And, on finding that many people had never heard of genetics, the team attempted to explain the concept.

This is a continuing process. One morning last November — seven years into the project — a community leader in Ibadan visited Owolabi's private clinic. He said tensions had mounted because people who had participated in the study wanted to know the results of their genetic tests. Owolabi replied that they were still searching for genetic markers that would reveal a person's risk of stroke, and that it might be many years until any were found. "But it's a heart-warming question," he says, "because if the people demand a test, it means the study is the right thing to do."

Discovering the genetic underpinnings of stroke is also complicated by the fact that it, like many non-communicable disorders, is caused by a blend of biological and environmental factors. Owolabi flips through a blue booklet of questions answered by 9,000 participants so far. It asks about everything from family medical history to level of education. Insights are buried in the answers, even without DNA data: the team found, for instance, that young Nigerians and Ghanaians who eat green leafy vegetables every day have fewer strokes[1]. And that's just the beginning. "You see the amount of data we have accrued," he says. "I don't think we have used even 3% of it, so we need to get more funding to keep the work going."

Owolabi's team is now applying for new grants from the NIH, Wellcome and other international donors to sustain the work after the H3Africa grant ends. And to make themselves more appealing to collaborators and donors, they're increasing the amount of work they can do in Ibadan. Until last year, most of the genetic analyses were conducted at the University of Alabama in Tuscaloosa. But last June, the University of Ibadan installed a computer cluster to serve the project, and three young bioinformaticians are now crunching the data. "The big-data business is happening now," says Adigun Taiwo Olufisayo, a doctoral student concentrating on bioinformatics. But he also admits that funds are tight.

Last year, other graduate students on the team began to extract DNA from samples so that they can scour it for genetic variants linked to strokes. In a room the size of a cupboard, a technician labels tubes beside a freezer. Coker Motunrayo, a doctoral student studying memory loss after strokes, sits on the counter-top because there's not enough space for a chair. She insists that the H3Africa project is a success, even though their genetics work has just started. "Compare this to where we were five years ago, and you'd be stunned," she says.

On the cusp

Perhaps the most advanced genomics facility in West Africa right now is located in Ede in southwestern Nigeria. At Redeemer's University, a private institution founded by a Nigerian megachurch, microbiologist Christian Happi is building an empire. Construction teams are busy creating a $3.9-million home for the African Centre of Excellence for Genomics of Infectious Diseases.

Happi strides across a veranda, and into a series of rooms that will become a high-level biosafety laboratory suitable for working on Ebola and other dangerous pathogens. Another small room nearby will house a NovaSeq 6000 machine made by Illumina in San Diego, California, a multimillion-dollar piece of equipment that can sequence an entire human genome in less than 12 hours. It's the first of that model on the continent, says Happi, and it positions his centre, and Africa, "to become a player in the field of precision medicine". Then he announces that Herman Miller furniture is on the way. If it's good enough for his collaborators at the Broad Institute of MIT and Harvard in Cambridge, Massachusetts, he adds, it is good enough for his team.

Happi plans to move his lab into the facility in a few months. But the team is already doing advanced work on emerging outbreaks. At a small desk, one of Happi's graduate students, Judith Oguzie, stares at an interactive pie chart on her laptop. The chart displays all of the genetic sequences recovered from a blood sample shipped to the lab from a hospital as part of a countrywide effort to learn which microbes are infecting people with fevers. Typically, doctors test the patients for the disease they think is most likely, such as malaria, but this means other infections can be missed. For example, the sequences Oguzie is looking at belong to the *Plasmodium* parasites that cause malaria, the virus that causes the deadly Lassa fever, and human papillomavirus.

Oguzie says that a few years ago, she was processing samples from a hospital in which people were dying because their fevers had confounded diagnosis. With the help of next-generation sequencing, she found that they were infected with the virus that causes yellow fever. She showed Happi the results, and he reported the news to the Nigeria Centre for Disease Control (NCDC), which rapidly launched a vaccination campaign.

This was exactly what Oguzie had wanted

54GENE

out of science. "I'm happy when I solve problems that have to do with life," she says. She worked hard throughout university in Borno, even after the terrorist organization Boko Haram started attacking the northern state. She heard bomb blasts during lectures and knew people who were shot.

Nevertheless, Oguzie finished her degree in 2011. She had a son a few years later and wanted to stay with her family in Nigeria, but she struggled to find a graduate institution that would allow her to excel in genetics. She had already begun searching for scholarships at universities in the United Kingdom, Australia and the United States when she found out about Happi's lab.

Happi had been persuaded to return to Nigeria from Harvard School of Public Health in Boston. The vice-chancellor of Redeemer's at the time was an influential virologist named Oyewale Tomori. He offered Happi a lucrative start-up package to build an environment similar to the one he had become used to at Harvard.

Soon after he joined the university, Happi won H3Africa grants totalling $6.8 million that have led to some impressive projects. For example, he and his collaborators mapped the spread of infections in the country's largest outbreak of Lassa virus[2]. He also won World Bank funding for an African centre of genomics. The grant is paid out incrementally on the basis of milestones such as training graduate students or researchers from another African country. So far, his centre has earned more than $9 million.

> "BLOOD IS A RESOURCE, WHETHER IT'S INSIDE HUMANS OR OUTSIDE."

He says the money means that he can offer experienced researchers salaries that stop them from leaving Nigeria and keep his lab up to date with the fast-moving field. Happi invites a rotating cast of top infectious-disease scientists from the United States to collaborate with his team in Ede. "I want to build a place where we can work together," he says, "not a place from where things are taken away."

But in an office beside Happi's, geneticist Onikepe Folarin says she has no time to conduct research because she's constantly writing grant proposals, and reporting back to donors on various milestones. To lessen their reliance on grants, she and Happi plan to start selling genomics services.

At the moment, African researchers pay a lot to ship samples and reagents to and from China and the United States, and these items often get held up at ports. But with his sequencing equipment and machines to produce important reagents such as primers, Happi hopes to provide a commercial service to other researchers on the continent — and use the money to fund his research.

Disruptors

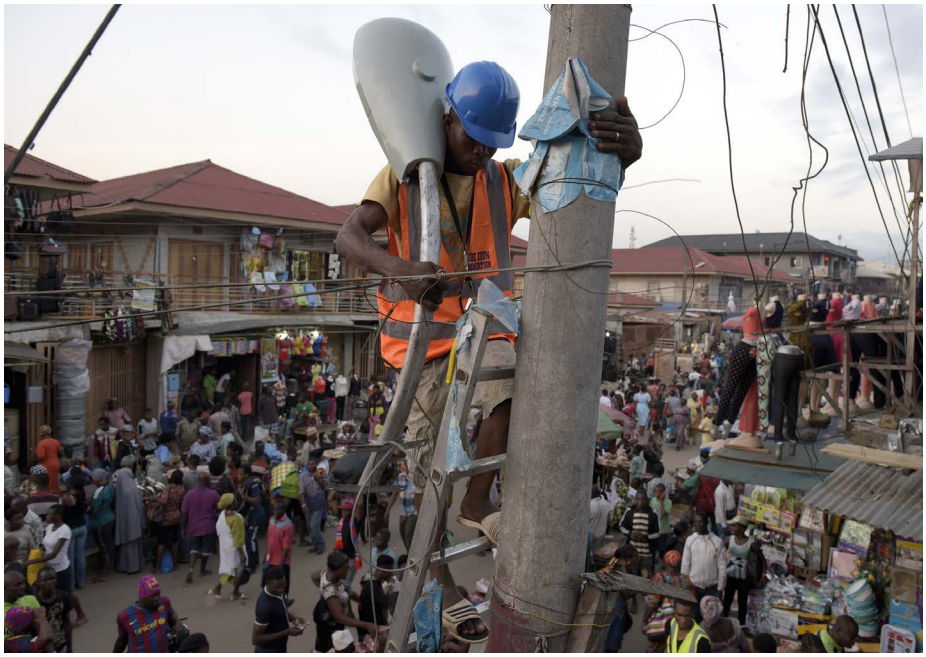
As the son of a plant geneticist, 54Gene head Ene-Obong developed a certain angst about the fits and starts of international grants. So after earning a PhD in genetics, he studied business with the aim of driving research sustainably. One idea he has for 54Gene is to charge drug-development firms for access to the genetic data in the company's biobank. This model has proved successful elsewhere. For example, last year, the UK Biobank received $120 million from 4 pharmaceutical giants for access to information on 125,000 people.

54Gene won't say how it is financing its study to analyse 100,000 genomes from Nigerians, but it has gained the backing of physicians from 17 hospitals across the country, who will send blood samples from consenting people with chronic diseases such as cancer, diabetes and Alzheimer's disease.

But as the first for-profit genetics endeavour in Nigeria, 54Gene must navigate uncharted ethical territory. People could feel cheated if they donate samples to research and then learn that the company turned a profit while they struggle to afford health care. Concerns about being taken advantage of loom large

AMY MAXMEN

Onikepe Folarin and Christian Happi stand in front of a soon-to-be completed genomics centre for studying infectious disease in Nigeria.



PIUS UTOMI EKPEI/AFP VIA GETTY

A perennial concern, Nigeria's underpowered infrastructure frustrates technology firms.

in Nigeria — and in Africa more generally — because of a history of the continent being exploited for everything from slavery to diamonds. As Anthony Ahumibe, the senior laboratory adviser at the NCDC, says: "Blood is a resource, whether it's inside humans or outside."

The concerns are well founded. Last year, for example, the Sanger Institute in Hinxton, UK, came under fire for licensing a gene chip based on African genome data to US biotechnology company Thermo Fisher, which was planning to manufacture the chip for a profit. This infuriated both the African researchers who had collaborated with the British team and the Ugandan study participants, who had not consented to the deal.

Seeing the potential for disaster, Aminu Yakubu, a bioethicist who helped revise Nigeria's regulations at the start of the H3Africa projects, offered to join 54Gene last year to help the company come up with solutions. "I understand why people will be sceptical, so we will be as transparent as possible, and sensitive to concerns about exploitation," he says. He and Ene-Obong are devising ways to give back to the public even before genetic discoveries are made. For example, they might donate dialysis machines to participating hospitals that lack them. "We are not just doing this to make money," says Ene-Obong. "As a private company, we need money to operate, but my goal is to study African genetics and translate the insights into products that help people."

The barriers

Unlike their younger colleagues, some established Nigerian researchers hesitate to celebrate the country's inarguable growth in genomics because they see obstacles in the path ahead. One of the biggest challenges is the lack of national funding. In 2016, it seemed that Nigeria's government was realizing the importance of research when it approved a measure to commit 1% of its GDP to science and technology. That would have amounted to $3.8 billion last year, but the money never materialized, and the research budget remains at about $750 million annually — the total across all fields.

Tomori compares this situation with that in China — another middle-income country. A decade ago, China's government plied the field of genetics with incentives such as tax exemptions and housing for scientists, and it put 2% of its GDP into research. Those investments have paid off; in 2018, China surpassed Europe in biotech investment.

> "IF WE SIT IN OUR LABS DOING THE SAME THINGS, THE SITUATION WILL NOT IMPROVE."

And because the Nigerian government does not fund much science, it has limited power to set research agendas. That could stunt genetics projects because the most powerful studies stem from long-term national initiatives, such as the UK Biobank and the China Kadoorie Biobank, says Prabhat Jha, an epidemiologist at the University of Toronto in Canada. Nigeria does have a few large biobanks, generally attached to specific research projects — and 54Gene's would add to that, but Jha warns that it's often difficult to cobble together samples from disparate studies because the data were collected with different aims. Creating a unified genomics initiative should be a priority, he says. "If there were good prospective studies under way in Africa," he adds, "we could really start to understand the key determinants of diseases and deaths there."

Even more basic problems stand in the way of success, not least the lack of a reliable electrical grid. "Until the government puts in basic infrastructure, we cannot move forward," says Tomori. In the meantime, institutes and companies are spending a huge portion of their budgets on back-up generators, diesel fuel and solar panels. According to a report released last year by the International Monetary Fund, Nigeria's inadequate electricity supply costs the country about $29 billion per year[3]. And in a survey by the Center for Global Development, Nigeria's booming tech sector named electricity as its number-one constraint[4].

To change the status quo, Tomori says, his Nigerian colleagues must persuade their leaders and the public that investments in science matter. "If we sit in our labs doing the same things, the situation will not improve," Tomori says. "We need to get out of our test tubes and talk about these issues."

But the director of genomics research at the Nigerian Ministry of Science and Technology in Abuja, Oyekanmi Nash, argues that government funding will flow more freely once science starts to deliver tangible benefits. He credits H3Africa with triggering the first steps. Now, he says, it's up to researchers to build on the effort and show how their science helps. Nash joined 54Gene's initiative to sequence 100,000 genomes because of the start-up's promise to translate genetics results into medicines. "Once we become strong enough," he says, "the government will listen."

It's a tough bet to make, especially given that Nigeria's post-recession economy remains sluggish. But the country's younger geneticists don't really have an option outside of optimism. "It's not been easy," says Ndodo. "Most of us have worked until the middle of the night, taken out loans to get training outside [Nigeria], and then come back to change the system." But, he says, scientists are on firmer ground than their predecessors. And they're driven. "No one else will tell our story," Ndodo says. "No one else will do research that targets our own interests."

Amy Maxmen writes for *Nature* from Oakland, California.

1. Sarfo, F. S. *et al. Stroke* **49**, 1116–1122 (2018).
2. Siddle, K. J. *et al. N. Engl. J. Med.* **379**, 1745–1753 (2018).
3. International Monetary Fund. *Nigeria: Staff Report for the 2019 Article IV Consultation* (IMF, 2019).
4. Ramachandran, V., Obado-Joel, J., Fatai, R., Masood, J. S. & Blessing, O. *The New Economy of Africa: Opportunities for Nigeria's Emerging Technology Sector* (Center for Global Development, 2019).