



# Facing up to genome injustice

*Scientists from under-represented groups are leading the push to make genomics more inclusive by working with communities that have been overlooked or abused.*

BY GIORGIA GUGLIELMI

**N**éstor Ruiz Hernández has been fighting for recognition for decades. He grew up in a town near the Pacific coast of southern Mexico, where he and many others trace their ancestry to enslaved people brought across the Atlantic Ocean from Africa in the sixteenth century. They consider themselves Afromexican, but the group is not officially recognized by the Mexican government as a minority ethnic group. If it were, community members might receive government funding for cultural and public-health programmes. As it stands, they're ignored.

Then in 2015, Ruiz Hernández met María Ávila, a population geneticist at Stanford University in California. Ávila wanted to analyse the DNA of people from Afromexican communities in Veracruz, Guerrero and Oaxaca states to identify the extent of their African ancestry. The project would prove challenging. When Ávila approached community members, she noticed that many couldn't read or write — and not everyone



Cristián, Genaro and Isidra (from left to right) are featured in a photography project to celebrate Afromexican culture in Coyolillo, Mexico. They are descendants of enslaved people brought from Africa in the 1500s.

identified as Afromexican. So she had to think carefully about how to report findings back to them.

Instead of providing numbers showing the percentage of African ancestry, Ávila opted for drawings of chromosomes in which each segment was colour-coded according to its ancestral make-up — green for African, red for Native Mexican, blue for European. “The researchers read the results to us and explained what each colour meant,” Ruiz Hernández says. “It turns out that my mother is Afromexican, but my father has Indigenous ancestry.” Ruiz Hernández, who identifies as “100% Afromexican”, didn’t expect this result, but he says he was happy with the study, and so were other members of his community who participated. “They asked questions, they laughed, they showed interest,” he says.

Ávila, who now leads a genome research group at the National Autonomous University of Mexico in Querétaro, is one of a growing number of researchers who are making waves in human genomics. These up-and-coming scientists, many of whom come from groups that are under-represented both in DNA databases and the research workforce, have made consultation and community involvement central to their work with Indigenous and other marginalized populations. They are publishing ethical recommendations<sup>1,2</sup>, launching training programmes for Indigenous people and leading the way in working with minority groups in genome research. The efforts are desperately needed, says Keolu Fox, a Native Hawaiian anthropologist and genome scientist at the University of California, San Diego. “The bar is so low currently that you need a shovel,” he says.

Building trust and establishing long-lasting partnerships with communities is not easy, and many in the field are still trying to figure out how to manage scientific goals and, at the same time, respect cultural sensitivities.

Fox worries that some still see Indigenous groups as guinea pigs rather than as research partners, an egregious approach that he describes as “bio-colonial”. But he is confident that the new generation of genome researchers will do better. “Younger people probably have more of — the Hawaiian word for this is *kuleana* — it’s your obligation to things,” Fox says. “Some are calling it ‘woke’ science.”

### NOT SO DIVERSE

For the past 30 years, human genomics has made exciting advances in reconstructing population history and identifying which genes make a person susceptible to a specific disease. But most genome studies have focused on people of European descent. An analysis published in March revealed that, as of 2018, only 22% of individuals in genome-wide association studies were of non-European ancestry<sup>3</sup>. People of African and Latin American descent and Indigenous people, together, represented less than 4% of participants (see ‘Missing diversity’).

There have been a number of efforts to increase genome diversity. In 2010, the US National Institutes of Health (NIH) and the Wellcome Trust in London launched the Human Heredity and Health in Africa (H3Africa) initiative, which supports Africa-led genome research. And last year, the NIH started enrolment for the All of Us research programme, which plans to collect DNA and health data from hundreds of thousands of people of varying ethnicities in the United States.

These programmes are “a very good start”, says H3Africa founder Charles Rotimi, a Nigerian genetic epidemiologist at the National Human Genome Research Institute in Bethesda, Maryland. Rotimi, who in the 1990s led the first efforts to include African populations in large-scale genomics projects, says that at the time there were just a few geneticists who looked like him. More than 20 years on, “we’re doing a better job, but we could do much better”, he says.

The reasons behind the lack of diversity in genome research are many. But they include a past fraught with abuses by Western scientists. One infamous tale involved Arizona State University researchers, who in the 1990s took DNA samples from members of the Havasupai Tribe in Arizona for a study on diabetes, but later used the samples without the tribe’s consent for studies on schizophrenia and patterns of population mixing and migration. In 2010, the Havasupai won a US\$700,000 settlement, and the university was forced to return all the samples it had collected.

Concerns about the misuse of DNA have caused some communities to refrain from participating in genetic studies. And scientists can be hesitant to reach out, even to those groups that are willing to take part. Without formal training on how to work with Indigenous or other marginalized people, “some researchers feel at a loss and just go for an easier population”, says Jennifer Raff, an anthropologist and geneticist at the University of Kansas in Lawrence.

A handful of Indigenous and non-Indigenous scientists are trying to stop this cycle of disengagement. In 2011, Ripan Malhi, a molecular anthropologist at the University of Illinois at Urbana–Champaign, launched the Summer Internship for Indigenous Peoples in Genomics (SING). The yearly, week-long course is taught mostly by Indigenous faculty members, and enables people from Indigenous communities, including students at tribal colleges and universities, to learn about genomics and discuss its uses and misuses. The workshop was initially funded by the US National Science Foundation and the University of Illinois; it is now supported by the NIH.

Since its start, SING has trained nearly 150 participants and expanded to New Zealand and Canada. Some of its alumni have gone on to obtain PhDs in genetics and to start their own laboratories. Katrina Claw, a Diné/Navajo genome researcher who will join the University of Colorado Anschutz Medical Campus as an assistant professor this August, was a graduate student at the University of Washington in Seattle when she attended the first SING workshop. It helped to shape her career, Claw says. “I had never been in a space where there were other Indigenous students who were interested in genomics.”

After completing her PhD, Claw stayed at the University of Washington and studied why some American Indian and Alaska

## MISSING DIVERSITY

Geneticists have struggled to better represent humanity's diversity in genome-wide association studies, which can reveal important information about genetic contributors to health risks. Most of the data used in such studies as of 2018 came from people of European descent.



SOURCE: REF. 3

Native people metabolize nicotine faster than do people of other ethnic backgrounds. Claw has also teamed up with Nanibaa' Garrison, a geneticist and bioethicist at Seattle Children's Hospital and a member of the Navajo Nation, to interview Native American leaders, educators and community members about their concerns, and to ask for suggestions on how to improve genetic research in tribal communities.

The outcome of that survey is not yet published. But Garrison, who's helping the Navajo Nation to develop regulations that would allow genetic research on tribal land after a 17-year ban, says that the results are likely to inform tribal science policy. "If tribes feel empowered to make decisions for themselves, rather than relying on other people, that may lead to greater engagement," Garrison says.

### NOT DISAPPEARED

As a member of one of the smallest minority groups in the United States, Krystal Tsosie knows what it feels like to be ignored and "have your viewpoint being invalidated because people believe that you have disappeared". That's why she advocates for Indigenous people to become equal partners, rather than just participants, in genetic research.

Tsosie, a Diné/Navajo geneticist at Vanderbilt University in Nashville, Tennessee, is working with the Turtle Mountain Band of Chippewa Indians in North Dakota to investigate the genetic factors that might explain why, within the community, some women are more susceptible than others to pre-eclampsia. The condition causes high blood pressure during pregnancy and increases the risk of seizures and premature birth.

The study was started about 15 years ago by Lyle Best, a family practitioner in the Turtle Mountain Indian Reservation. In 2017, Best, who had moved away from the reservation, was looking for somebody to take over the pre-eclampsia study, and Tsosie was seeking a PhD project focused on Native Americans. "It was great timing," Tsosie says.

Now she supervises the genetics laboratory at Turtle Mountain Community College in Belcourt, North Dakota, and collaborates with the tribal-research review board, which vets research protocols and ensures that the tribe is represented appropriately in project publications.

Tsosie also tries to engage the broader community in the project, for example by inviting research trainees to give interviews on local radio. So far, more than 40 tribal college students have worked on the pre-eclampsia project, Tsosie says.

Stacie Blue, a Turtle Mountain community member and a natural-resources instructor at the community college, says that the students in her general-biology class are excited about the pre-eclampsia project. "They see tribal researchers participating in the science and leading it," she says. "It's empowering; it's huge."

Despite being a relatively new concept in genomics, community-based participatory research is picking up steam. Raff, for example, has been working on a project born out of a discussion with the elders of the Iñupiat people of the Arctic Slope in Alaska.

A few years before Raff joined the University of Utah in Salt Lake City as a postdoctoral fellow, members of the Iñupiat had asked the research community for archaeological support in excavating the remains of their ancestors, which were falling into the ocean as a result of coastal erosion. The community was also interested in doing DNA analysis of

the remains, so they started a collaboration with Dennis O'Rourke, an anthropologist and Raff's postdoctoral mentor.

"The project was completely driven by the community," Raff says. Local students excavated the remains, and tribal members consulted with the scientists about how to conduct the project. During those discussions, one of the elders asked Raff to analyse the DNA of current members of the community, too. As a result of that request, Raff and her colleagues developed another project in which they compared the DNA from Iñupiat ancestors with that of contemporary people to study the population's genetic history<sup>4</sup>.

"The important thing is to ask and find out what could be useful to communities and build that explicitly into your project," Raff says.

Malhi uses a similar approach. As soon as he starts a new collaboration, he works with community leaders on a written agreement that details the expectations of both the community and the researchers. "Once we have that, that's great because we know what to expect from one another," he says.

The work is not without challenges. The biggest one is time, Malhi says. Once researchers have a result, they can't just publish it. Instead, they have to go back and ask participants for feedback. "We've got to make sure that we're not going to say anything that may be detrimental to the community," Malhi says. This iterative process can take several years, and sometimes community leaders decide that they want to take a break from participating. Malhi says that one of his projects has stalled for more than six years. That can be hard to reconcile with research

grants that are awarded for only a limited amount of time. "The system is not set up for community-based research," he says.

Genome scientists also have to be careful about communicating results on sensitive issues such as the migration and mixing of people, says Deepti Gurdasani, a genetic epidemiologist at the Wellcome Sanger Institute in Hinxton, UK.

As part of her postdoctoral studies with population geneticist Manjinder Sandhu, Gurdasani has been involved in several research projects covering regions of Africa torn by recent civil wars. To avoid fostering violence, the group talks extensively to community leaders to understand their perspective before communicating results on population history. "We also engage local university researchers and field staff — they're very aware of the local sensitivities," she says.

But even when populations agree to participate in research, scientists still have to obtain consent from individuals, says James Suzman, a social anthropologist in Cambridge, UK, who leads a consultancy that advises businesses and governments on the impacts of their programmes on southern African communities.

In 2016, Suzman, who has worked with San communities in southern Africa for nearly 30 years, held a workshop to develop a standard research consent process for two particular groups. After two days of discussions around genomic research, community leaders told Suzman that they didn't understand the genetics and would rather have a trusted person to negotiate study participation for them. Suzman says that picturing DNA or cells can be very difficult "if you haven't seen them through a microscope or you haven't had them presented in a school book". The lesson, he says, is that obtaining genuine consent "is a hell of a lot harder than most of the funders of this kind of research imagine".

*"The bar is so low currently that you need a shovel."*



Native Hawaiian anthropologist Keolu Fox aims to set up a network of research centres led by different Indigenous communities.

### MIX AND MATCH

Once every few months, Maanasa Raghavan, a human geneticist at the University of Chicago in Illinois, travels to India to hold public discussions about genome research. There, she is joined by Niraj Rai, a researcher at the Birbal Sahni Institute of Palaeosciences in Lucknow, who in 2017 set up India's first laboratory for studying ancient DNA. A question that the pair often gets asked is how different populations compare with each other genetically. "That's a very valid question," Raghavan says — one that got her into population genomics.

Indian populations are highly genetically mixed. "We have extreme diversity," Rai says. But how and when the mixing happened remains unclear. Rai and Raghavan hope that putting together ancient and modern genetic data sets from India will help them to get a better understanding of how some South Asian populations formed. After approaching leaders from rural and urban communities around India, the duo meets with them to talk about research projects and find out questions that people would like to see answered. "Many people are interested in where they come from and who their ancestors were," Raghavan says.

One of the communities that Raghavan and Rai work with is a group of Telugu-speaking people who live in a small village near Guntur in Andhra Pradesh. About 50 families in the village practise Judaism, and most of them can read and write Hebrew, says Sadok Yacobi, the group's spiritual leader. Yacobi says that community members are descended from the Tribe of Ephraim, one of the ten lost tribes of Israel, and he hopes that analysing the members' DNA will help them to be recognized as Jews. Nearly 200 people who have given blood samples are now eager to learn about their ancestry, Yacobi says.

Beyond answering questions about heritage, research on population history has the potential to inform studies on health issues. In 2009, genetic epidemiologist Marlo Möller and her colleagues at Stellenbosch

University in South Africa teamed up with Brenna Henn, a population geneticist then at Stanford University who had been studying the genomes of southern African individuals who have KhoeSan ancestry. Their hope was to find out why people with this background are more susceptible to tuberculosis than are other groups<sup>5</sup>.

Henn and her collaborators have since partnered with ten rural health clinics in the Northern Cape province of South Africa, where incoming patients are asked whether they want to be involved in the project.

After almost two decades of working in southern Africa, Henn, who is now at the University of California, Davis, says that she still worries "about a lot of things" — from representing the communities correctly in publications and protecting the privacy of participants to making sure that participation is voluntary.

Researchers and members of Indigenous communities are trying to provide help for those wrestling with these issues. Groups in Africa and New Zealand have issued guidelines in the past few years that call for inclusion and equity in genomics research<sup>6</sup>, and leaders from three San groups in South Africa have developed their own code of research ethics. Members of the SING consortium published recommendations for conducting genetic research in Indigenous groups last year<sup>2</sup>. But research funders, publishers and most governments have no standard requirements for scientists working with Indigenous populations. "It would be very nice if there was one set of guidelines that fit every population, but not all groups are the same," says Sarah Tishkoff, a human geneticist at the University of Pennsylvania in Philadelphia, who in the 1990s pioneered efforts to work with African populations in genomics. "It's very hard to come up with a 'one size fits all'."

Journal publishers are not always aware of the sensitivities in publishing some data. It then becomes a task that falls to those asked to review papers. "I want to see multiple privacy and consent forms, one written in the local language and one written in English," says Fox.

He adds that it's crucial for the benefits of genetic research to trickle down to study participants. "If a pharmaceutical drug is developed around a certain genetic variant that is discovered in a community, you want to see that money go towards the development of clinics and educational programmes and hospitals and libraries in that community," he says.

Building research infrastructure on Indigenous land would also "de-black-box" genetic technologies and create transparency about the projects, Fox says. That's why he's now raising funds to launch an independent research institute for genetic research in Indigenous communities. Fox hopes that, over time, the project will become a network of research centres in different Indigenous communities, with independent biobanks, computational clusters and fellowship programmes. "We're trying to move towards things that have 100% Indigenous leadership," he says.

Ávila, like many of her contemporaries, feels a sense of responsibility. She says that one of her goals is to give more visibility to Afromexicans. The country's population census didn't list 'black' as an ethnicity option until 2015, says Heladio Reyes Cruz, who coordinates a non-profit organization that promotes conservation and community development in Santa Rosa de Lima, Oaxaca. "Scientific research is useful for visibility, because academics are able to publish and be in the media, which is something that local leaders usually struggle to do," Reyes Cruz says.

Ávila says she's been in contact with advisers to the Mexican government who were interested in knowing more about the ancestry of Afromexicans. She hopes that her research will help them in the recognition process. As a scientist, she says, "I do see an opportunity to do things better than in the past". ■

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