Q&A

How two researchers built the first genetics cohort of African children with autism

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In 2015, **Maria Chahrour**, assistant professor of genetics and neuroscience at the University of Texas Southwestern Medical Center, began recruiting participants for studies on autism genetics out of her lab in Dallas. Among those who responded were parents and families who had recently immigrated from East Africa. They wanted to join the study, but they had some concerns and questions. So they asked if they could form their own group, in which they could help create the rules around how their data would be collected and used.

The collaboration that bloomed from those conversations created the first cohort of **African children with autism** — one that continues to grow and recruit families around the globe. Chahrour and her research partner, Leah Seyoum-Tesfa, spoke to *Spectrum* about their experiences forming the cohort and why increasing genetic diversity is vital for autism research.

> Listen to the interview here, or read the transcript below or **download it here**. **https://www.spectrumnews.org/wp-content/uploads/2021/02/Spectrum-interview-2.11.21.mp3**

***Spectrum*:** Could you both tell me who you are and what you do?

Maria Chahrour: Okay, well, hello, everyone, and thank you for having us. My name is Maria

Chahrour. I'm an assistant professor at the Eugene McDermott Center and the neuroscience department at UT Southwestern Medical Center in Dallas. My lab studies the genetics of autism. We want to find the genes that cause autism and to study their function in depth, so that we can understand the specific biological pathways that they function in. And ultimately, we hope that our work will inform diagnosis and therapies.

Leah Seyoum-Tesfa: My name is Leah Seyoum-Tesfa. I'm originally from Ethiopia. I live in Irving, Texas. I am a mother of four children, two of whom are on the autism spectrum. In 2011, I started a nonprofit organization called **Reaching Families Advocacy and Support Group**. The purpose of the organization is to work with East African families who have children with intellectual and developmental disabilities. The organization started in Dallas, Texas, but it's spread to — we have several organizations all over the United States. By training, I'm a nurse and I was a nurse practitioner. But I work, currently I'm an advocate. I support families in various systems — in the medical, educational, as well as the social systems. I also provide community awareness about developmental disabilities all over the United States.

I enjoy working with families; it's a very rewarding thing to be able to support families' access [to] early intervention and see the progress that children made throughout the year. And I support families also and their children to adulthood.

S: Thank you both for joining us, and you both do really interesting work, so I'm excited to talk about how you work together. Could you tell me a little bit about how you first met each other and came to work together?

MC: Sure. So in 2015 I moved to Dallas to start my own lab. And, as I said, a big part of our mission is to identify causative genes in families with autism with a specific focus on Dallas' diverse population. So I had an ongoing human genetics study, recruiting local families with autism, and someone from the Ethiopian community in Dallas found out about the study. He actually works at UT Southwestern as well, and he saw one of our flyers and told Leah about the study, and then he introduced us. And I guess, Leah, I would love to hear how that initial reach-out happened for you and what was your impression when you heard about the study?

LS-T: When Dr. Bogale [Aredo], who was the president of [the **Ethiopian Health Professionals Association**] — I am a member of that group — reminded me about this study, and he saw the flyer and he showed it to me, I was very interested, because I've been concerned about the number of children that I see that have, from the East African community, primarily with autism. I've felt for a while that we are seeing a higher prevalence in our population. And we also see more-affected children in our population. So when he showed me the flyer, I was very interested because our community wants to find out why the higher prevalence and if there's a genetic connection in our community. So I contacted Maria, and our collaboration started from there.

S: How did you come to collaborate rather than just participating in the study? Did you initially set

out to want to have a bigger role in the study, or how did that relationship come about?

MC: I was really interested and impressed with everything that Leah had been doing and all of her efforts in her community. And you know, we had all these discussions about what she found with the higher prevalence of autism in East African families as she was working with the community. And we started having more and more of these meetings and discussions, and it sort of organically, I guess, grew into a collaboration. It was, I would say, a mutual learning journey for both of us, you know? I was really fascinated with all of the aspects that she was an expert in. And vice versa, I think.

LS-T: I agree with that. Yeah, it was a learning experience for me as well. Because other than the research that I have done as part of my training at the **LEND** program — I had attended a training in 2013, and my project was on the prevalence of autism in the East African community in Texas. I had taken data from the Texas Education Agency, and I had found that it was a higher prevalence. And this came when I met Maria; I was very interested in studying this further.

S: I think Maria had told me previously that once you wanted to include more people from your community in the study, that there were some questions that came up about participating, and it actually spawned its own separate cohort study instead. Can you tell me about some of those questions that came up? And then how that led to a separate study being made for the African community around autism?

MC: So, as I mentioned, you know, the two of us started meeting and discussing the study designs and what elements we had to take into consideration. So, specifically, the community's concerns about privacy and data protection and the stigma associated with autism within the community. I visited the community center and church multiple times, spoke to family members about autism and genetics, and about the study that we were running. And, you know, myself and Leah, we answered their questions and addressed their concerns. And I would say, then, we took care of some logistics. Before I go into that maybe I'll let Leah tell you a little bit more about the families' specific concerns around these issues.

LS-T: There's a lot of stigma around it. And people are very careful to admit their children have autism, or a family member. Unfortunately, it's associated with mental health issues, and somebody being crazy, or somebody being like an evil spirit. So the stigma around it was a big issue that we have to deal with, and I still deal with in the community. The other concern was lack of knowledge. They didn't know what research would mean. It's not something that we've participated [in] as a community in the DFW area, or even any area that I'm aware of as an immigrant community. So doing a study was something new.

S: And DFW, is that Dallas-Fort Worth?

LS-T: Dallas-Fort Worth, I'm sorry.

The other piece was, what is going to come with this study? What's the outcome and what the data was going to be used for?

S: And so, what kind of things did you do, both in the recruiting and in the study design, to kind of allay those concerns?

MC: I would say we really had a lot of discussions. A critical part of this was just meeting with family members, addressing all of their questions, making sure that everyone is comfortable with everything we had in the study forms. Leah had reviewed all of the study forms. And we translated them into Amharic and Tigrinya. And then after we finalized all of these logistics, Leah announced the start of recruitment and enrollment to the community members and the families that she was supporting through the Reach foundation. I would say it took us about two years from when we initially met, to set everything up and have all of these really important and critical discussions with community members so that we can incorporate their feedback, before we actually started actively enrolling participants.

S: Wow, two years. That's a long time.

MC: Yeah.

S: And so what has the recruitment process been like since then? You know, how many families have you been able to recruit and is it still ongoing? Catch me up to how it's been going the last couple of years.

MC: This past year, it's been really slow, of course, with everything that's going on with the **COVID-19 pandemic**. But you know, so far we've enrolled 30 families, I would say, and that's over 120 individuals, and it's still very much ongoing and active.

When UT Southwestern shut down earlier in March, human subject research that did not involve a critical procedure was kind of put on hold. So we couldn't bring in study participants for their research appointments. I think that was the main hit. But now, you know, we're hoping that things are going to get better, and that we're able to deal with all of these logistical issues. We're all adapting, I would say.

S: So, Leah, you told us at the beginning about what Reach does. Can you tell me how that plays a role in the study that you do with Maria?

LS-T: I work by bringing community awareness. I go to several churches — before COVID. Now

through Zoom, I do community awareness; I teach families about early signs of autism. And the purpose is to get early intervention. At that time, I do offer all the families an opportunity to participate in the study. And not all families are ready to do that. They're still trying to accept that their child has autism. We're also going through the difficult diagnostic process, finding a diagnostician and waiting on these long lines with the various providers. So it takes a little bit longer. I think within a year after the diagnosis, a lot of families will agree or decide to participate or not.

So the purpose, as I said, is to provide early intervention and help families, but as part of that I do explain to them about the research and the opportunity to join the research. Like I said, it's not every family that chooses to participate. But some families are very interested; some choose to just do a genetic study through their pediatrician or specialist. But that's how we are able to reach families. Now I do have — like I said, I started with families in [the] Dallas area — but I do have families, we even have some families in Europe, that live in Germany and I think other countries, that were able to participate in this study.

S: Wow. Do you have partners in Europe that sort of help with the recruitment there?

LS-T: No, I do 100 percent of the recruitment, families that I support through accessing interventions. We do have a heavy online presence, and through our website, and through our Facebook and other resources, we provide information. We have monthly educational meetings that are available to any families recorded. We teach them about various things about early intervention, about therapies, about [**applied behavior analysis**], about all kinds of things, dietary interventions. We have specialists that come and speak to families about, the bigger one is a lot of behavior support. Fortunately, we do have many community members that are in the profession that are able to share this information in Tigrinya and in Amharic that is very accessible to these families. So families from all over the world, we have families in Africa as well, in Asia; people, immigrants, families can access our educational information. And part of that educational information is we had Maria speak about the genetic study, and they can access that and reach Maria at UT Southwestern to participate in the study.

MC: Once we make contact with the families, you know, my study coordinator sort of arranges for the research appointment if they're local, or otherwise we send them a study kit with instructions of what to do and how to actually collect samples and things like that.

S: And when you're doing this global outreach, are you mostly focused on families from Ethiopia specifically?

MC: So we're focusing on East African families, specifically from Ethiopia and Eritrea, although we've had Kenyan and Somali families participate as well. But the vast majority are from Ethiopia and Eritrea.

LS-T: We do support, actually, Kenyan families. There's not a heavy presence in the DFW area. But we do have a mother that supports the Kenyan families, and through her we were able to recruit a few families I believe, but it's heavy Ethiopian, Eritrean immigrant families in the DFW area.

S: And you have a partner in Ethiopia, correct? An organization there that you partner with?

MC: It sort of started as this part of our long-term capacity-building project for autism in Ethiopia. So I got to **visit the Joy Autism Center** in Addis Ababa in the summer of 2019. And I discussed our study with the center founder, Zemi Yenus. And as part of that trip, I also gave a talk and ran a workshop with colleagues on autism and autism genetics at the Bahir Dar University, and that was geared towards healthcare professionals. So Zemi is interested in collaborating with myself and Leah, but we haven't actually started enrolling participants simply because of logistical issues that were caused by the pandemic and the recent political unrest. Of course, we are planning to expand our study and collaborate with colleagues and community partners in Ethiopia. That's our long-term plan.

S: And so now that it's been going on, the study's been going on for a few years, what have you been hearing from families about their experience participating in the study?

MC: I believe they're excited about the study. We've had a meeting after we completed the latest batch of sequencing to discuss our preliminary analysis with the community. And we're planning for other community update meetings as we finalize our analysis. But I think Leah can speak more to the family's impressions and how motivated they are to participate.

LS-T: The ones that have participated are very eager to know the results. They call me often and say, “What have we found? Where are we now?” They're just eager to find out; the process was very easy. Maria really made it easy in that the kit was sent home; when we were drawing blood, the phlebotomist came to the home to draw the blood. And it was really a very smooth process for a lot of the families, even the ones in Europe. They told me the process was very easy. And we're just waiting for the results. Everybody's eager. We are realizing the prevalence; we're seeing a lot of our friends and siblings also having children with autism. So that's what we really need to know, if there is a genetic connection here.

S: I'm curious if you've seen any kind of shifts, like you mentioned that there's some stigma in the community or just not being as familiar with research studies. Have you seen, anecdotally, shifts from people who have participated in any of those attitudes?

LS-T: You know, I see a change in that even families that have not participated in the study are now very interested in doing that. Initially, people were worried about what's going to happen with the data — is my name is going to be available on [the] internet about my child having autism? — those kinds of concerns. But now that they know, and Maria has come and explained to us how the

data is saved, there are more families interested. Because of COVID, there's a lot going on with the disability community. COVID has been even harder. Families are struggling with kids not attending school. So it's kind of been really hard. And then finding even somebody to diagnose the children during this time has been difficult.

But I've seen a shift. I've seen a shift in stigma, because there's so many of us, many centers all over the United States, that we are going to the churches and talking about autism. We're in a good place; I think we're going in the right direction. Kids are getting help sooner.

S: It sounds like a really powerful community-based approach to doing this kind of science.

MC: Yes, yes, for sure.

LS-T: Definitely. Definitely.

S: And maybe we can talk a little bit about, you know, what you're finding from the study. What kind of gaps is that filling for the science about autism?

MC: Populations in Africa are the most genetically diverse in the world and carry up to three times as many rare variants as, say, populations of European origin. And research so far on the genetics of autism has overwhelmingly focused on people of European ancestry. And, of course, although these studies are extremely valuable to our understanding of this complex genetics of autism, they don't really capture the genetic diversity on the African continent. And this loss of genetic diversity in the current studies really limits our scope of understanding autism.

So because genomic studies so far have been largely focused on European populations and identifying autism variants in these European cohorts, the transferability of these findings to non-European populations is limited.

And then, of course, as genetic findings move into the clinic, this lack of diversity and lack of genetic data from non-European populations translates to healthcare disparities. So when a genetic diagnosis is made in the clinic, it's vital to understand the variant in the context of ancestry, because the frequencies of some of these variants are population-specific.

So for clinical genetics to be equitable, it needs to be able to offer patients and their families interpretation that encompasses their specific ancestry. And as a genetics community, the community as a whole recognizes this need for diversity and the need to do more sequencing on the African continent to be able to understand variants in the context of ancestry, and is working to be more inclusive. An example of this, you know, there's a big effort right now that's focused on exactly doing this. And it's the Human Heredity and Health in Africa, or the **H3Africa consortium**, which was conceived to address the paucity of genomics research in Africa. So I think we have a lot to learn from this. We have a lot to find and discover. And we have this amazing opportunity to

do this now.

LS-T: We realize there's a very heavy burden of more affected children in our community. I strongly believe in that. We're seeing more kids in our community. Siblings — I have a lot of families that have two, three children somewhere on the spectrum. I myself have two kids on the autism spectrum, fraternal twins. So we are very eager to find out what is causing this high incidence of autism in our children. And hopefully, this research will answer some of our questions.

MC: I just want to add to that we are really interested and we set out to see: What is this genetic factor that's predisposing the community to autism? And that's sort of the big question that we're going after.

S: When you say there's a higher **prevalence** in the community, what kind of numbers would you say there are?

MC: Leah's own work on public schools in the state of Texas showed that the prevalence is up to three times higher than the prevalence in the general non-African population. And also, there is one of the sites where the [Centers for Disease Control and Prevention] does the monitoring network for autism is in Minnesota, and they found that the prevalence of autism **in the Somali population** in Minnesota was, I believe, up to two to three times higher than the general population as well.

So there are all these findings that were pretty much from prevalence studies that were done on immigrant populations outside of Africa because, unfortunately, I believe there are only two prevalence studies for autism in Africa — one out of Uganda and one out of Nigeria. You know, of course, depending on who you ask, there might be other factors that influence or result in this higher prevalence. And of course, these prevalence studies on immigrant populations are smaller than what you would typically see from other prevalence studies. But we think it's a start. We think that in the meantime, we can do something with the information that we already have. And you know, as a geneticist, I'm really interested in the genetic risk factors. Although we're not eliminating other hypotheses, of course, but we're testing our hypothesis that there is a genetic risk factor in this community

LS-T: And the study that I did, it wasn't published, but it was part of my report. In the Amharic-speaking population, we saw 1 in 40. In the Tigrinya-speaking, we saw 1 in 51. And in the Ethiopic — they call it Ethiopic because there's other languages spoken in Ethiopia, including Amharic, Tigrinya, Oromo — 1 in 22 children had autism.

And then in the whole Texas population, at that time is 1 in 167 children were identified — educational identification of autism, with my research. And then, as Maria mentioned, we reviewed a lot of studies that were done in Europe. And there's also a study out of California that showed

higher prevalence in immigrant families who have children with autism who are African American. The **European studies** looked in depth about **East African families**. There was also a New Zealand and Australian study that had **higher prevalence** in our community.

S: Wow, those are some very big discrepancies. Very big differences.

LS-T: There was, there was. And you know, the other thing is, this is in educationally identified children. They were looking at the children that are, they tend to identify the more affected children. And the kids that are less affected are not identified, even so in our community, because parents don't want their children identified. If there's a little bit of, you know, social problems, and the kids end up being verbal, they usually don't want their kids identified. These are kids that have significant disability and are often educated separately in a self-contained classroom.

So we're looking at even a much higher rate in our community, because we're not always identifying all the children. This was, if you look at the Somali study in Minnesota, the first study came out in 2014. Those identified were 100 percent of those children had intellectual disability. Whereas a much lesser number of children in the Minnesota study of the other races had intellectual disability. What that tells me, and I think the researchers concluded, is that we're not identifying those kids that are less affected in these communities. We're just looking at those with intellectual disability that are easily identified in the school system.

MC: Yeah, yeah. So, you know, basically, we're missing a lot of kids who are more mildly affected. And I think that, again, speaks to this really big need for doing comprehensive prevalence studies in Africa.

LS-T: Definitely, definitely.

S: And does your genetic study mostly then lean toward having people who have intellectual disability? Or are you also working to identify those less affected kids and get them in the study as well?

MC: So we do have kids on both ends of the spectrum, I would say. It's because these families were primarily identified through Leah's efforts in the Reach foundation, and she works with all kinds of kids on the spectrum. So, you know, we are enrolling everyone at this point, yeah.

LS-T: We do have the same, even people, families that come to me for help, usually have more affected children. These kids are identified early on; usually they're all over the spectrum. But the older kids that are identified usually are more significantly affected that come to me for help.

S: So just thinking about the more broad need in the field to have greater diversity in genetic studies, are there any kind of lessons that you think you've learned in creating and working on this cohort that might inform other researchers about how to increase diversity in genetic studies?

MC: Yes, this is a big question. And we could both go on and on. So we certainly learned a lot. For one, we need to continue doing this and expand our study to enroll more participants and sequence more genomes. And the genetic diversity on the African continent can teach us a lot about the genetics of autism and about the biological pathways and mechanisms underlying the disorder.

We learned that there's still a lot of stigma associated with having autism in many communities. And we need to really be diligent about removing that stigma and spreading the right information so that we can empower families to deal with this in their communities. And we need to listen to, understand and respect the communities' concerns. And we need to work together. It has to be a true partnership between scientists and parents for us to be successful. We also learned that a lot of these families are facing and dealing with the burdens of autism without much support. So participating in research studies may not necessarily be a top priority when you don't have access to basic services.

LS-T: Yeah. You said it really well, Maria. Families are struggling, caring for the kids and accessing resources. Sometimes research is not a priority for them. I think the fact that Maria was able to come and explain everything really well for us, that was very helpful. And she also had an opportunity to come back and update us about where the research is. And we were able to recruit more families after that.

I think just understanding their culture and the stigma around it was very good for Maria to understand and work with us [and make] research easy for the families. She accommodated the needs of the families, because it would have been very hard for the families to take their kids to have their blood drawn, the whole family; she made that very easier. And those things are very important. Making things very accessible for the families and continuing to communicate with them. It's very important, especially for communities that are not, might not have a lot of knowledge about research.

S: Great. Well, this has been a really fascinating discussion about your work. I'm really curious to see where it goes in the next couple of years.

MC: Thank you. Yeah, we're both really excited about this, and hopeful.

LS-T: And thank you for giving us the opportunity to share our research and about our concern in our community.