VIDEO TRANSCRIPT

Exploring Difference in the Biology Classroom - Complexity in Human Genetics

Link to video.

[**Rob O'Malley**]: Okay. Hello, everyone. Welcome. I am Rob O'Malley of the Personal Genetics Education Project, or PGED. My pronouns are he and him, and I am a middle-aged white man with light -grade hair and a beard.

On behalf of PGED and our collaborators at the Center for ELSI Resources and Analysis, and our invited speakers, it is my pleasure to welcome you to today's program. Please feel free to introduce yourselves and chat and share what part of the world you call home.

PGED is based in the Department of Genetics. at Harvard Medical School. We strive to support inclusive and impactful genetics engagement that is people -centered and multidirectional. We seek to empower individuals and communities to share and learn from each other, to advocate for themselves in decision -making, and to enrich science as a whole, including in the practice and translation of research, in science education, in public discourse, and in policy.

Educators have been our long -standing and valued allies in this work. That is why we are excited to be partnering with CERA to bring you today's program, the fourth and final session in our four -part webinar series, Exploring Difference in the Biology Classroom. Prior events are viewable online at ELSIhub.org on representing wide -ranging family structures and personal identities using the latest pedigree number, on engaging with genetic disability and difference, and on what genetic ancestry tests mean and what they don't.

The title of today's session is "Beyond Mendel, Leading with Complexity When Teaching Human Genetics." Teaching Mendelian patterns of inheritance is a useful way to introduce basic genetic concepts in the classroom.

However, I'm sorry, have I been muted this whole time? Just the last couple of seconds. Okay, sorry, sorry.

So in this session, researchers will share insights to guide teaching about human genetics with a focus on complexity. Presenters will discuss ways scientists are trying to uncover and quantify the contributions of many genetic loci to common diseases, some limitations to such approaches and current understandings of how genetic and environmental factors, including social factors, interact to produce health outcomes.

We know this is a challenging time to be a teacher for many reasons. Among them is a demanding task to keep up with constantly evolving language approaches and content, particularly when it involves how we talk about people. Accordingly, we greatly value your choosing to spend time with us today. We hope today's session will provide some useful ideas to support better pedagogy around what can be complicated and challenging topics.

We're also incredibly grateful for our speakers who have deep expertise in understanding and communicating the complexity of genetic mechanisms, their relationship to health, and exploring these processes within a cultural and historical context. Thank you again for joining us.

And with that, I'll hand these over to Dr. Sandra Soo-Jin Lee to share about CERA to share some housekeeping and a code of conduct for our time together, and to introduce the speakers.

[**Sandra Soo-Jin Lee**] Thank you, Rob. Oh, it's so great to see all the introductions in the chat. I'm seeing Barbados and Los Angeles and Portugal. So welcome, everyone.

I'm Sandra Soo-Jin Lee, co-director of the Center for ELSI Resources and Analysis, or CERA, and professor of Medical Humanities and Ethics at Columbia University.

And I'm delighted that you have joined us for the final ELSI Conversations event in this series. As Rob mentioned, it's entitled "Beyond Mendel, Leading with Complexity When Teaching Human Genetics."

This session will run for one hour, and after the session ends, we invite you to stay for an optional discussion from 7 to 7:30 Eastern Time on Classroom integration strategies that will be facilitated by PGED. If you're interested and available to join that, please stay on this call.

So in this session, we will hear from presenters and we're very, very fortunate to have two excellent speakers today.

Shaniqua Collier, who's an associate professor with tenure in the department of clinical research. and Leadership at the George Washington University School of Medicine and Health Sciences, and Dr. Emer Kenny, Professor of Medicine and Genetics at Icahn School of Medicine at Mount Sinai. She is also the founding director of the Institute for Genomic Health.

The last half hour after our presenters presented will be dedicated to audience Q &A. And I'm gonna tell you in a moment what we hope you'll do in terms of submitting your questions.

But for those of you who may be new to CERA, we provide resources to support research on the ethical, legal, and social implications of genetics and genomics and serve to connect scholars, educators, scientists, and others. members of the public, and others to engage ELSI issues. CERA is funded by the National Human Genome Research Institute at NIH and is managed by teams at Stanford and Columbia universities in partnership with the Hastings Center and the PGED team at Harvard.

We encourage you to join the CERA mailing list to stay up to date on future events on this collaboration series, as well as other ELSI conversations and access the resources that will be mentioned in today's session.

You can probably see the link in the chat. And note that all links mentioned in today's session, this includes speaker and moderator biographies as well as other resources will be part of the recording.

So just a little bit of housekeeping. This session will be recorded and uploaded to ELSIhub.org. You will be able to access the recording after the session ends.

And you can do that by signing up for the CERA Newsletter where the link to the recording will be distributed in a post event email. Or you can visit the Exploring Differences in the Biology Classroom page on ELSIhub.org. The recording and resources will also be sent out by email tomorrow to all registrants and attendees in today's session.

So today we also have a professional live captioner present to provide captions for today's session. And if you want this please click on the link in the description bottom of the screen to access closed captioning. Please note that if you do not activate the closed captioning at the bottom of the screen, the live captions won't show up so please do click it if that's what you would like.

Please also use the chat box to ask questions. We will post links to references as I mentioned, but you should also feel free to add your own references to share them with others that are in the Zoom room. If you have any questions during the session, please email us at info@ELSIhub.org.

So with that, I'm very happy to hand it over to our speakers today, and I'll hand it off first to Shaniqua.

[**Shaniqua Collier**] Hello, everyone. I'd like to thank the Personal Genetics Education Project and ELSIHub for the honor of engaging with you tonight. Can you hear me all right?

[**Rob**] Yeah, you're great.

[**Shaniqua**] Okay, great. I'm an African American woman with dark brown hair that I happen to be wearing straight and glasses. I do not have any conflicts of interest to declare and the opinions expressed are my own and should not be construed as the views of my affiliate institutions or collaborators.

I will start by highlighting areas that seem to cause a great deal of confusion and that require clear communication about the complexities of environment, race, and health. I speak using an ELSI lens, understanding that the only way I can do this is to make sure that the overwhelming majority of us want to improve the well-being of society. But, there is genuine debate about how to describe genomic and environmental influences.

So I will start with genomics and difference. You have likely heard one or more of some version of these statements. First, the Human Genome project revealed that we are over 99.9 % the same. Yet we are most interested in the 0.1 % difference in variation, representing 3 million points on the genome that could have important implications for health and treatment outcomes.

Second, while there is more similarity across racial groups than within them, race and racism have social impacts that affect health and disease.

These nuances may confuse students and they may hear contradictory messages. Many medical textbooks, for instance, have a long history of suggesting race -based medicine. Some professors may point to genetics as a contributing factor to racial health disparities.

The NASEM ad hoc committee on population descriptors in genomics describes the historical confounding of race genetics and environment and recommends the next steps forward. I highly recommend that you read it if you have not done so already.

Today I will provide a few examples, illuminating some of these complexities I describe. And also my concerns about rendering people, identities, biological factors, and environmental influences invisible, as well as some obstacles to communication.

First on race and ancestry.

This is a compelling image published in a paper by my colleagues at the Center for Research on Genomics and Global Health. It uses different colors to represent 21 different ancestries determined from 282 global populations.

The figure simultaneously shows ancestry mixture within each individual population and geographical region. Each small horizontal line in this figure represents an individual and each ancestry that every individual has is colored.

The figure illustrates continuous genetic variation among populations rather than sharp boundaries between continents, ethno-lingual groups, races, or ethnicities. It conveys recent and historic admixture. It is also noteworthy that the authors discovered three previously unknown ancestries through their sampling.

Due to non -existent sampling in some parts of the world, there still may be ancestries that remain unidentified.

Second on the environment, differences in politics geography, social influences, also confound environments. Most of us are familiar with some version of these statements. Minoritized and marginalized people disproportionately live in disadvantaged and toxic environments.

These inequities are based on social, political, and economic forces, including systematic racism and colonialism. From these statements about the statistics about racial disparities, students may take away that race is a good proxy for studying environmental factors and that we can use race or ethnic group categories to account for the environmental factors that are difficult to measure.

However, this is a communication breakdown that overlooks aspects of the environment that cause racial disparities. Of course, we know it's true that racialized minorities are more likely to live in neighborhoods with less access to high-quality schools and food, safe recreation, clean air, and water, and that these environments profoundly impact physical and mental health. These are injustices that society needs to target and eliminate.

When considering my area of work, genomics and ELSI, where we often focus on the interactions between social forces and genomics, race is too often used as a stand-in for these environmental factors and for specific environmental factors.

When we say, for instance, that black patients are more likely to experience hypertension because of their environment, what about the environment raises the risk? Is it access to food and doctors, educational attainment, something else, or a combination of these factors? In some cases, the relevant factor may be racism.

When a social determinant of health such as racism is a contributor to poor outcomes versus biology, we need to know when and how to develop interventions and communicate that to students.

The author here reported that racism is linked empirically with depression, anxiety, stress, other mental health outcomes, and poor general and physical health. Notably, racism is not just a US problem. Some form of racism occurs in different countries, and for many different groups.

Educators should discuss the profound effects of racism on health in lessons when they're thinking. about and considering gene-environment interactions, teaching about racial inequities without considering racism, or the broader social context may inadvertently train students to over-emphasize race, and underappreciate the profound influences of social forces like racism.

I will now give examples of what we miss when we conflate race, environment and genetics, especially when we use broad population labels. I will start with a historical example.

The island of St Helena in the Atlantic Ocean became a common drop-off point for people freed from slave ships as the slave trade neared its end. Evidence shows that slave ships brought to St Helena originated in Central and West Africa, and that some individuals came from as far away as Mozambique and Madagascar. DNA sequencing confirmed that those buried there were from different parts of Africa.

However, the research team could not determine their likely ethnicities. Burial site DNA samples did not match current-day African reference samples.

Slavery stripped people of their identities but also caused historical gaps in our understanding of different African identities. We risk perpetuating such gaps, unless we ask who is rendered invisible in our research and education. And have our students ask such questions.

Broad population descriptors can obscure biological differences. This figure provides an excellent example within the context of pharmacogenomics.

Medically relevant differences in allele frequencies exist among the Luya, the Masai, and Yoruba, who scientists are likely to label collectively as African ancestry populations. There are also medically relevant differences in allele frequencies found between Chinese, Japanese, and Gujarati Indians, who scientists often describe as Asian ancestry populations.

A broad population label can also suggest that a research study is more representative than it is. Dr. Perry Payne found, for instance, that an FDA alert for carbamazepine relied on only two of 37 countries in Asia to conclude that patients across broad areas of Asia are more likely to have the relevant alleles.

This map shows the areas where the drug label warning applied with the excluded continents and countries marked with X's. Such reporting may help protect drug companies from liability or reflect understanding about genetic similarity, but contains nuances relevant to how we define inclusion and representation. Using continental and racial labels to describe genetic differences can also lead to unequal funding, attention, and understanding.

Sickle cell disease was widely labeled as a black disease historically, although it affects patients from Sub -Saharan Africa, Spanish -speaking regions in the Western Hemisphere, India, Turkey, Greece, Saudi Arabia, and Italy.

Also there's often confusion between sickle cell trait, which occurs when a patient inherits one gene that causes sickle cell, versus sickle cell disease, which occurs when patients that causes sickle cell, which occurs when patients inherits one gene that causes sickle cell, it is poorly understood.

And many have argued that it is poorly understood because it has been racialized. I also want to draw attention to the drawbacks of making assumptions about race and environments.

For example, the Black Progress Report describes an investigation of associations between specific attributes and life expectancy, noting that we miss opportunities to understand factors correlating with thriving in black communities, especially when we focus on making black -white comparisons. Another example is portraying Asian Americans as homogeneous model minorities. This describes an association between the Black Progress Report, the systematic exclusion faced by different Asian communities and the role of different and sometimes moderating environmental factors.

In conclusion, I am concerned that these issues are present -day phenomena in the public and in our labs. In the outside world, white supremacists use science to promote racist ideologies such as racial purity. Some estimate that 35 % of the world's population can drink milk and does not have lactose intolerance. And it's not specific to white patients. Much of the global population experiences some type of lactose intolerance.

Inside our own house, our labs have cracked foundations. Isabella Wilkerson’s warnings for America that I listed here also apply to our fields.

So I'm going to end there my sincere thanks to you and to my colleagues at CRGGH who provided feedback on this talk and a space where we often have conversations about this topic. Thank you. I'll hand it over to Dr. Kenny.

[**Eimear Kenny**] Thank you very much and I'm going to share my slides and I just want to apologize to everybody online. I live in New York and there's a fire truck just outside my window beeping very loudly. So you may hear some background noise. Okay.

Okay, can everybody see my slides.? Yes. Perfect. Thank you.

So thank you to Dr. Collier. That was wonderful. And I'm going to take the baton now and maybe pivot a little bit toward thinking about how some of these ideas and concepts play out as we apply genomic information in arenas, particularly, of health and health care.

Oops, there we go.

And before I start, I just want to mention my disclosures. I receive personal fees from a number of industry companies. I have received research funding from one specifically, Allelica, and I serve on the advisory board for Encompass Biosciences, Overtone, and Gallateo Bio.

So I just want to sort of situate us by pointing out the degree of plummeting of cost of sequencing that has occurred over the last two decades.

Indeed, sequence technology has reduced so quickly in terms of cost of a single genome. It has surpassed our ability to generate compute capacity. That's the famous Moore's Law.

And even more interesting, you'll see toward the end of that graph there, you see a sort of a plateau out over the last about five to eight years.

But in the last year in particular, there's more excitement again in terms of new technologies that's going to see that cost plummet even further. And we're really in sort of 22 and 23 looking at the emergence of many new different types of chemistry for sequencing that will bring the cost of a genome, at least the genome substrate down to in order of hundreds, maybe down further than that in five years or so to tens of dollars, making genetic sequencing potentially one of the cheapest tests for any

health system, which starts to raise the question about who will have their genome sequenced in the future.

And if we think about the potential for using genomics in health care, we can think about the genome as a blueprint for our own individual DNA, and that information could be used in myriad different clinical contexts and settings to ask many different questions over the course of an individual's life.

But in practice, what we face are a number of obstacles and barriers to using this information well and appropriately.

And one of them is that what we know most about genomics is based predominantly on individuals of Northwest European ancestry.

And relative to the global population, we know little from other populations around the world. Certainly, many other populations are relatively underrepresented and there are populations in the world for which we know almost nothing, if anything at all, about human genetic diversity.

And this issue of lacking diversity is not just one for the genomic research field, but it also goes through the entire pipeline of how we bring new knowledge into clinical practice.

It includes our clinical trials, including far little far too little diversity, and the fact that a lot of research is centered in high-resource areas of the world, and other areas of the world lack resource and infrastructure to be a part of the research.

So with all that in mind, let us think about where we will start to see genomic information increasingly be used in clinical care. You know, there's a lot of excitement and emergence in terms of technology and innovation.

And it is true that genomic information is used in some arenas of clinical care predominantly for rare diseases that are suspected to have a genetic underpinning in arenas, some arenas of oncology, autoimmune disease and pharmacology, where I

think we'll start to see genomic information increasingly come in as we start to get more and more genetically targeted therapies, and if we start to use liquid biopsies for early detection of cancer.

One other area of great excitement in terms of potential for how we can bring genomic information into more routine clinical care, particularly for more common diseases, is in the arena of preventive medicine, which typically includes the incorporation of aspects of clinical history with family history and social determinants of health or lifestyle factors, and how that impacts an individual's risk for disease. There is increasing interest in adding information from each individual's own DNA to enhance the prediction of disease risk.

And the idea is that this may happen within the next five or 10 years that we will start to see this information being used more routinely in preventive medicine.

So how would that play out? Well, let's take a simpler example. There's no simple examples, and this is a series on complexity, but a simpler example is what we call monogenic risk,

which is the type of risk for some diseases where there's a single variant in a single gene that confers a greater risk than a single gene. disease that it is associated with.

So one example of this is I think something that many on this group will have heard of or know about. These are the BRCA1 and BRCA2 genes related to cancer risk.

And many women in particular who are at high family and clinical risk for breast or ovarian cancers may be able to access screening for variants in these genes just as part of their healthcare.

However, if you flip the paradigm and start asking in just a normal population of individuals, how many people who harbor a pathogenic variant in one of these genes are even aware of their cancer risk?

The answer is about 74 % of people who harbor a pathogenic variant in one of these genes are unaware and, worse, often don't become aware until after a diagnosis of cancer has occurred.

And so this raises the possibility that we could maybe introduce screening for genomic risk earlier before symptoms and signs of disease occur to help us better manage, monitor, surveil, and intervene at earlier stages of disease to improve preventive medicine. And this particular example is also very interesting because these risk variants vary a lot in terms of different families, communities and populations in terms of prevalence, and they don't just impact women. In fact, there is a range of cancer risks that we learn increasingly about over the years, including cancers that impact males, including male breast and prostate cancer.

So now let's think of a more complex genetic risk. And this is now at a genome level, what we call polygenic risk scores, which are small effects across many variants and many genes in a genome that collectively increase or decrease any individuals risk for common diseases relative to others in the population and as clinicians what we might like to know is who in the population would sit at the high the highest level of risk in a population so we can start to consider that information in health management.

And polygenic risk, at least in human populations, is relatively new for reasons that we needed to have databases of observations of genetic variation in humans linked to health outcomes for millions or hundreds of millions of individuals before we had power to use this information for out of sample risk prediction.

But in the last four or five years as a field and a research community, we've really come to that point. So there is a lot of enthusiasm and momentum around how we will bring this type of information into preventive medicine.

And here's an example of how polygenic risk will play out in comparison, for example, to monogenic risk for disease. And this is looking at heart disease or cardiovascular disease.

And we know there are rare monogenic variants underline a condition called familial hypercholesterolemia. One in 200 of us anywhere in the world, more or less, have a chance to harbor one of these pathogenic variants. And these variants confer a three to five fold increased risk over that person's lifetime of developing heart disease and related symptoms.

However, using these more genome scale aggregate polygenic risk methods, we can actually identify larger populations, in this case, 8 % of individuals who have the same higher risk, but the genetic predictor is starting to predict more people in the population that we can start to tailor health management strategies for.

However, again, we're back to some of the issues and barriers of using empirical data in very data driven ways to produce products that could be used in medicine.

And this is that the polygenic risks using this information need to be trained on existing data that we have. And as you start to use them in individuals who are less represented in that training data and more divergent from that training data, you start to see that the accuracy goes down.

So this is really because of the bias and skew toward representing Northwestern Europeans in our training data set and not representing or under representing other human populations around the world.

And we can do things to fix this issue and I'll point out this work is from the lab of Seijin Fatoumou, where we can start to change the training data.

For example, if we wanted to create a test for predicting polygenic risk in for African and African descent populations, then we might want to use African American and African descent data in the training and we can see when we do that that we improve the prediction accuracy in this case for predicting total cholesterol level.

However, just tuning and calibrating the predictors and building more generalizable and transferable predictors on the genetic side is not going to fix the whole piece of the pie.

Because when you look even more closely and this is in the same paper using that predictor in two different populations across the continent of Africa. One being a South African Zulu population and one being a population from an urban center in Uganda, you see the performance of those particular predictors are wildly different.

And although this study did not make it, many social determinants of health, we can in these models understand that what we're seeing is an environmental effect and hypothesize that there is social determinants of health that are going on that have much bigger impact across these population groups than the genomic predictor and not bringing those into a model actually is the thing that's determining its accuracy.

So if we think about what is impacting genetic risk in humans, it is inextricably linked to our own human history and dispersal around this planet and the environments that we live in today.

And this combined impact of ancestry and social determinants help, that's what needs to be understood, not only the genetic component, if we want to understand, equitable risk prediction for preventive medicine measures, and this highlights really a need for translational research that not only incorporates social determinants of health, but also incorporates diverse populations across the whole pipeline for discovery and translational research.

And I'll just end by pointing out the growth in genomics and healthcare around the world. This is a snapshot from 2019. And you can see the many regions of the world and countries of the world that are making major investments in bringing this type of information into the care of patients. And the last thing I want to leave us all with as we move into the Q &A is really paraphrasing a friend and colleague, Vence Bonham, from NHGRI who said this, which I think really gets to the kernel of the issue, which is that bringing genomic information increasingly into clinical care may not ameliorate current health inequities, because for the majority of people, the biggest slice of the pie is our environment. that we are surrounded by, our access to health care, and the degrees of racism and other social determinants of health we experience in our life.

For some people it will, if some people have rare but penetrant genetic disorders, but for the vast majority of us, the genomic component is gonna be a small piece of the pie that is working together with all the other components that impact our health.

However, if we do not increase diversity in genomic research and in the types of translation and implementation, then we will likely increase inadvertently current health inequities by producing tools and products and tests that are not generalizable or transferable to any human on the planet.

And with that, I'll end there and join you all in Q &A.

[**Rob**] Thank you so much to Shaniqua and Eimear for those presentations giving us a lot to think about.

I do, we're gonna shift out of Q&A. I do encourage you if you have questions to drop them in the chat box. We have some questions that came up beforehand in registration and we'll work through those as well, but I'll just be keeping an eye on chat as new questions come in.

So I thought maybe I'd start with just one very central question, which did come up in a lot of the comments in registration, which is this issue of sort of... threading the needle between the need to cover like in, you know, in high school biology or in like introductory biology context, the basics, you know, hundred squares and purple and white flowers and smooth, you know, smooth or wrinkled peas, which kind of presents some of the framework of Mendelian genetics balancing that with grappling with the very complex realities of even monogenic risk in the context of, how do we even know what we know? How generalizable is our knowledge about genetic risk with some of these issues that maybe people will actually grapple with in their lives?

Do either of you have suggestions about sort of... how to engage with recognizing we have to cover some of that, that educators will have to cover some of that fundamental principles? How do we pull in some of this reality of the incredible complexity when we're talking about human genetics in ways that are accessible, that stick with people,

that maybe can help inform how they're thinking about these questions in their own lives?

That was maybe a long -winded question, but I hope you get the gist of it.

[**Eimear**] Well, maybe I can start, Shaniqua, and I think that these very basic principles of Mendelian inheritance that you're discussing are, they remain important to teach. Biology is not a science that has necessarily first principles, but we have good foundation and learnings that are important as basic principles of the field that I think it is still important to teach.

But I think what is also important to teach layering onto that is that we have good foundation and learnings that are important to teach is to move away from the simple model, which does allow basic concepts to be taught, but is actually the less common case in human populations in reality. There's actually very few diseases that are 100% penetrant and expressive in humans.

There's a couple. I mean, we can point to things like Tay Sachs, for example, would be one example where we could point and we could say that that looks a little bit like that.

However, the vast majority of diseases where there is a heritable component are very variable in the degree to which there's heritability. And that's the most common scenario. And that's how we have to think. about genetics as we think about how it impacts human populations.

[**Shaniqua**] Thanks, Dr Kenny, for that answer and I'll just add, you know, coming from an LC perspective there's just been so much more discussion since the start of the genome project, and the funding of ELSI research about these complexities and there are more resources that educators can access about these complexities as well that I think could be brought into the classroom and it would provide opportunities for students to have conversations about scenarios to help illuminate some of the challenges related to talking about genetics and the environment.

[**Rob**] Lawrence did you have a question? We actually prefer things in chat but Lawrence if you're very brief you could you could share.

[**Lawrence**] I will just be very brief, and I'll just give you a brief way to talk about this, and that most people know the phrase "the exception that proves the rule". Mendelian inheritance is the exception, but we're teaching the exception the way to phrase it is, so what is the rule? And the rule is that most things aren't Mendelian. And I think that helps teachers think about... how to address the bigger picture, maybe get away from the exception because most traits aren't Mendelian. And most things are not penetrant. So thank you for letting me not chat, not type.

[**Rob**] I appreciate that. Thank you. Yeah, so I think maybe a related question in thinking about sort of how teachers will be trying to maybe grapple with these more complex elements of genetics and how they apply to humans.

Is there a popular misconception that you've encountered in your own maybe teaching or in conversations with different audiences with policymakers perhaps related to human genetics that this may be really central for educators to be thinking about, like if they're at that intro bio level or, you know, high school biology level, like a really common misconception that that educators should have in mind about addressing.

[**Shaniqua**] I could start. I think I often hear the phrase that race correlates with continental ancestry. And so one of the points I wanted to make sure I made was that that kind of statement or understanding doesn't help us really think about the genomic variation within continents.

And so it's important to recognize that we are obscuring or not thinking about differences. Or even the many populations that we, in Saudi Arabia, in the Middle East, for example, or in Central Asia, that we need to include more in research. And so that's one I often think about.

[**Eimear**] Yeah, I think that's a very good one to think about and I think not just in genetics research in epidemiological research in many other areas of research,

we see this come up over and over again. But, you know, in genetic research, we maybe have a little bit of an advantage that we can follow the specific variant,

and that teaches us that these terms that we use, like race or instead of race as continental ancestry, are often not complex enough to actually capture the impact of specific variants or specific polygenic risk scores in humans.

And I think, you know, sometimes we may do this in research maybe because we feel that's the limit of the information we've collected or sometimes maybe even for shortcuts, but you know when you really start to try and think how this impacts human either in public health settings or in medicine or clinical settings then you start to see that the degree of shortcoming in that that approach.

[**Rob**] Yeah, thank you both. Oh, here's a question that came in during chat. This is very topical one. How well do you feel that NIH is all of us project and we can maybe layer on other kind of efforts to diversify genetics research will make a dent in the diversity of genome-wide data.

[**Eimear**] I could start with that one. So, you know, the NIH's all of us project really set out from the onset to increase the representation of different diverse communities across the US in that research project.

And it was a stated goal from the outset. And, that makes it unfortunately quite unusual still today in terms of large publicly funded research projects.

Although many funders and many researchers themselves are really trying to move in that direction, but I think all of us really does stand out in that regard. And, you know, I guess as I alluded to in my talk, genomics is a very empirical research discipline. And we make statements based on empirical associations and observations. And so having a greater degree of representation in a large, well -funded, well -resourced research project like all of us, I think, will make a great impact in terms of discovery and application.

[**Rob**] Okay, great. And as people may know, there has been some big advances in just in the last couple days related to better understandings of the diversity of human genomes and efforts to address some of those issues. And we'll, I think, maybe share some materials about that with attendees after the session.

I want to-- another question that came up in registration that we've sort of engaged with a little bit through your presentations would be thinking about case examples in, from your work or others-- work you're familiar with that help really kind of illustrate the real complexity of like many health conditions or understanding risk.

You talked about, for example, the association with cancer with those particular gene variants. Would you encourage educators to be thinking perhaps about like that as a case study to delve into further?

Are there others that you think might have utility in sort of helping educators grapple with this idea of kind of leading with complexity, emphasizing complexity and in understanding genetics and health?

[**Eimear**] Well, I thought Shaniqua had some really nice examples there. One I would add is or one is sort of which is one of my go -tos to help exemplify complexity is the APOL1 locus.

So for those who may not be familiar with this, APOL1 is a gene that was discovered in African -American populations a little over 10 years ago.

And the reason that the study was performed in African -American populations is because there were known prevalence's in difference for chronic kidney disease and end -stage renal disease and related disease in African American populations.

So the groups that discovered this gene went looking for genes that might be driving that. And they found one. And this turns out to be a very important gene because it's got unusually for something that's quite common. So it's the risk, haplotypes are in about 13 % of African -Americans that we've looked at, but it actually has a large effect. And those are sort of the golden goose of genomics research where you find

something that's shared by a lot of people and has a large effect. That means that it has the biggest impact if we understand it better and we understand what it's doing.

So subsequently, others have looked within other African descent populations,

mainly from the constant of Africa and other African American communities across the US and shown similar effects and started to understand the the greater degree of diseases and conditions that this one gene risk alleles impact, including heartbeat hypertension, ischemic stroke and others, and the types of interactions with social determinants of health that impact the what we call the penetrance and the expressivity of that effect.

However, if you actually look at the sharing of those risk alleles around the world without assuming that it's only African and African descent populations that are impacted, you will learn that there are many people around the world who harbor this risk allele, and mainly due to African ancestry shared back through history from certain parts of Africa, whether or not they themselves identify as African descent today, who are completely understudied for this condition, for whom we know very, very little. Likewise, on the continent of Africa, these risk variants are only common in certain places.

So that, I think, is a good example of exactly Shaniqua's point, not making generalizations and associations, how that can actually hold us back from doing research where we need to do it to understand the impact of genetics in health outcomes.

[**Shaniqua**] That's a wonderful example, Emer. And it really is a modern day case of something that's labeled as an African American condition or issue, and it has huge implications in kidney transplant scenarios to name one example, where you will hear individuals debating whether or not you should treat a patient differently because they identify as African American and this link with what we're labeling as an African American issue, when there are just so many individuals who could possibly require an intervention that we might overlook.

[**Rob**] And if I could add to that, my understanding is that there are criteria that have been racialized, right, in terms of who's eligible for kidney transplants and who's not that have recently been revised and is drawing on some of these kind of outdated racist concepts of human difference as it relates to racial groupings.

[**Shaniqua**] So you're referring to EGFR scores and if any of you look at your lab reports that might be a part of routine kidney lab testing, you'll see that there's a regular score and then there's a score if you're African American and that was recently changed. And on my last lab report, it said that LabCorp is considering new configurations that don't take into account race. But for a long time, doctors might discuss treatment options or make referrals or wait to recommend getting on the kidney transplant list based on that score.

[**Rob**] Yeah. Wow. Well, looking at time, I think that we want to shift into wrapping up this component.

I do want to pause and just give a heartfelt thanks to both of our speakers, Dr. Shanique Collier and Dr. Eimear Kenny, and invite you to share any final takeaways or reflections very briefly before we wrap things up.

[**Shaniqua**] This was wonderful. It was wonderful to participate. Thank you.

[**Eimear]** Likewise. Thank you very much and thank you for your questions. Okay. Thank you both. So we're going to shift now to a discussion of classroom integration strategies.

And we invite everyone to join as we reflect and we'll be a little bit more conversational in tone as we think about incorporating this into classrooms. And so I'll welcome back Sandra now to share some closing remarks from CERA before we make that shift.

[**Sandra**] Yes, thank you for a wonderful session. Thank you, Eimear and Shaniqua. Before we transition into the next half hour of discussion, which will be moderated by PGED's Gill McNeil, I'd like to share some resources with you that will be dropped in the chat.

We wanted to thank you for joining us for the final event of this collaborative series and invite you to subscribe to our newsletter for the latest news on the next ELSI Conversations series as well as other resources mentioned in today's session and more announcements.

You can also find a curated set of resources on ELSIHub for educators on ELSIHub.org that will also be dropped in the chat.

And then finally, we really greatly appreciate your feedback. We take this very seriously and would love to hear about your suggestions for topics and speakers.

So please do fill out that survey. And with that, I'll hand it over to Gill McNeil, who will guide us in the discussion on classroom integration strategies.

Just as a reminder, this part of the event, this conversation will not be recorded, but please do join us there.